Epidemiological studies of bovine digital dermatitis in pasture-based dairy system in New Zealand

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Abstract

Bovine digital dermatitis (BDD) is an infectious disease of the feet of cattle. Worldwide, it is one of the most commonly observed foot diseases on many dairy farms, and is the most important infectious cause of lameness in cattle in confined dairy system. Although BDD is generally less common in pasture-based dairy system it can still cause significant production losses and welfare issues, in such systems.

This thesis contains seven original research works covering the epidemiological aspects of BDD in pasture-based cattle in New Zealand. Firstly, cross-sectional and longitudinal data obtained from Taranaki were analysed to identify the factors (including climate) associated with the disease. This was followed by a large scale cross-sectional study covering four regions in New Zealand looking at the prevalence of and risk factors for BDD. A longitudinal study was then undertaken on three farms in order to collect disease data (including BDD lesion type) over a lactation. Using this dataset, a deterministic compartment model was built to study the transmission dynamics of BDD within a dairy herd in New Zealand. Along with these large studies, two small validation studies were also carried out. The first study evaluated the agreement between two trained BDD observers in determining BDD presence/ absence in digital photographs, while the second one evaluated the reliability of clinical examination of BDD lesions in the milking parlour without prior washing of the animals' feet.

This work suggests that BDD has spread widely across New Zealand, although it has yet to reach the West Coast. In the four regions where BDD was identified, true between herd prevalences varied by region (from ~ 40% to > 65%). Furthermore, although BDD was found in many herds, true cow level prevalence was low in all affected regions, being generally less than 4% in affected herds. Several biosecurity-

related management practices were repeatedly identified as factors associated with increased BDD prevalence at both the herd and cow level. These included mixing heifers with animals from other properties; purchasing heifers for replacement and using outside staff to treat lame cows. In addition to the identified management practices, climate (rainfall and soil temperature) was also found to have had a significant association with the prevalence of BDD.

These studies used examination in the milking parlour as the method of identifying BDD lesions. This method while the best method of lesion detection for large scale studies is not perfect. It generally requires that feet are washed prior to examination, as lesions masked by dirt are difficult to identify. Our study quantified the effect, under New Zealand conditions, of feet washing prior to examination finding sensitivities of 0.34 (95% credible interval [CrI]: 0.088-0.69) and 0.63 (95%CrI: 0.46- 0.78) for pre- and post-washing, respectively. There was a 93.95% probability that the sensitivity of examination post-washing was greater than that pre-washing.

Limited information on the reliability of examination in the milking parlour prompted comparison of two trained observers using digital photographs. Agreement between the two observers was good; we could be 75% sure that the two observers had almost perfect agreement and 95% sure the two observers had at least substantial agreement.

It is crucial that since examination in the milking parlour is not a perfect reference test for detecting BDD lesions that when estimating prevalence, the sensitivity and specificity of this method is factored into the analysis. This is often achieved using an approach based on the binomial distribution. However, as the dairy herd is a finite population and the sampling of animals for BDD lesion is effectively

sampling without replacement, the correct distribution to use is the hypergeometric one. This is computationally complex so the Bayesian superpopulation approach was developed to allow continued use of the binomial distribution. The superpopulation approach was used to estimate prevalence in this thesis, one of the first uses of this approach in the veterinary field.

The appearance of BDD in New Zealand is different from that elsewhere. Most lesion have been observed are small grey, rubbery lesions which may or may not have thickened, darker edges. Less commonly larger, more proliferative lesions can also be found. Red active lesions are extremely rare. Post-treatment lesions are not a feature of the disease in New Zealand as lesions are treated only very rarely. Thus modelling approach used a BDD score system which focuses on early stage of BDD. This found that in infected dairy herds, although BDD prevalence will tend to increase year-on-year it is likely to remain relatively low (<18%) even after 10 years of within-herd transmission. It is likely that the low transmission rate during the late lactation (model assumption) results in more cases resolving than developing during this period and therefore results in the low prevalence of infectious cattle at the start of each subsequent lactation. Cattle with larger, more proliferative lesions had a stronger influence on the establishment and maintenance of DD than cattle with small lesions highlighting the importance of targeting these animals for intervention.

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List of Journal Articles

1. Yang, D.A., Gates, M.C., Müller, K.R., Laven, R.A., 2019a. Bayesian analysis of herd-level risk factors for bovine digital dermatitis in New Zealand dairy herds. BMC Veterinary Research 15, 125.

2. Yang, D.A., Johnson, W.O., Müller, K.R., Gates, M.C., Laven, R.A., 2019b. Estimating the herd and cow level prevalence of bovine digital dermatitis on New Zealand dairy farms: A Bayesian superpopulation approach. Preventive Veterinary Medicine 165, 76-84.

3. Yang, D.A., Laven, R.A., 2019a. Detecting bovine digital dermatitis in the milking parlour: To wash or not to wash, a Bayesian superpopulation approach. The Veterinary Journal 247, 38-43.

4. Yang, D.A., Laven, R.A., 2019b. Inter-observer agreement between two observers for bovine digital dermatitis identification in New Zealand using digital photographs. New Zealand Veterinary Journal 67, 143-147.

5. Yang, D.A., Laven, R.A., Chesterton, R.N., 2019c. Effects of climate and farm management practices on bovine digital dermatitis in spring-calving pasture-based dairy farms in Taranaki, New Zealand. The Veterinary Journal 247, 75-80.

6. Yang, D.A., Laven, R.A., Heuer, C., Vink, W.D., Chesterton, R.N., 2018. Farm level risk factors for bovine digital dermatitis in Taranaki, New Zealand: An analysis using a Bayesian hurdle model. The Veterinary Journal 234, 91-95.

List of Conference Papers

*** speaker in oral presentations**

1. Yang, D., Laven, R.A., Vink, W.D., Müller, K.R., Chesterton, R.N., 2017. Modelling the temporal pattern of bovine digital dermatitis in Taranaki, New Zealand using a semi-parametric approach. 19th International Symposium and 11th International Conference on Lameness in Ruminants, Munich, Germany, Sep, 2017.

2. Yang, D., Laven, R.A., Vink, W.D., Müller, K.R., Chesterton, R.N., 2017. Bayesian Poisson-gamma approach to investigate effect of farm management on bovine digital dermatitis in Taranaki, New Zealand. 19th International Symposium and 11th International Conference on Lameness in Ruminants, Munich, Germany, Sep, 2017.

3. Yang, D.*, Laven, R.A., Vink, W.D., Müller, K.R., Chesterton, R.N., 2017. Prevalence and incidence of bovine digital dermatitis in Taranaki, New Zealand, 2015-2016: Descriptive statistics of a longitudinal observation. 19th International Symposium and 11th International Conference on Lameness in Ruminants, Munich, Germany, Sep, 2017.

4. Laven, R. & Yang, D.A., 2017. Monitoring farm and cow level prevalence of bovine digital dermatitis in New Zealand. 19th International Symposium and 11th International Conference on Lameness in Ruminants, Munich, Germany, Sep, 2017.

5. Yang, D., Laven, R.A., Vink, W.D., Müller, K.R., Chesterton, R.N., 2017. Monitoring farm and cow level prevalence of bovine digital dermatitis in New Zealand. 3rd International Conference on Animal Health Surveillance, Rotorua, New Zealand Apr-May, 2017

6. Yang, D.A.*, 2018. *Bayesian two-part model* to correct both herd and animal level misclassification errors. Science week 2018, Australian and New Zealand College of Veterinary Scientists, Gold Coast, Australia, Jul, 2018.

7. Yang, D.A.*, Laven, R.A., Chesterton, R.N., 2018. Effect of season and climate on bovine digital dermatitis in spring-calving pasture-based dairy farms in Taranaki, New Zealand. Science week 2018, Australian and New Zealand College of Veterinary Scientists, Gold Coast, Australia, Jul, 2018.

8. Yang, D.A., & Laven, R.A., 2019. Bayesian superpopulation approach to evaluate the ability of detecting bovine digital dermatitis in the milking parlour without washing cows' feet. 20th International Symposium and 12th International Conference on Lameness in Ruminants, Tokyo, Japan, Mar, 2019.

9. Yang, D.A., Johnson, W.O., Müller, K.R., Gates, M.C., Laven, R.A., 2019. Confirming freedom from bovine digital dermatitis of dairy farms in the West Coast region of New Zealand. 20th International Symposium and 12th International Conference on Lameness in Ruminants, Tokyo, Japan, Mar, 2019.

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1.1. Introduction

Bovine digital dermatitis (BDD) is an infectious bacterial disease which principally affects the skin around the hooves of cattle. The disease was first reported in Italy in 1974 (Cheli and Mortellaro, 1974) and since then has been reported almost worldwide, with cases being reported in North America 1980 (Rebhun et al., 1980), South America (Borges et al., 1992), Asia (Kimura et al., 1993), Africa (Van Amstel et al., 1995) and Australasia (Milinovich et al., 2004).

BDD is usually seen as an ulcerative or hyperkeratotic lesion on the plantar aspect of the interdigital cleft (Read and Walker, 1998). However, the appearance of BDD lesions is very variable as the lesions can progress and regress over time under both treated and natural condition (Holzhauer et al., 2008a; Holzhauer et al., 2008b; Krull et al., 2016). This has led to the development of classification methods to describe these different stages including a simple colour system (Laven and Proven, 2000), the Iowa scoring system which focuses on distinguishing pre-clinical and clinical BDD (Krull et al., 2016), and the most widely used system – the M-score (Döpfer et al., 1997; Berry et al., 2012). This M-score scheme includes six distinct classes (M0, M1, M2, M3, M4, and M4.1). Class M0 is described as skin where lesions are macroscopically absent, class M1 as an active granulomatous area of 0 - 2 cm, class M2 as an ulcerative lesion of > 2 cm, class M3 as an ulcerative lesion covered by a scab, class M4 as alteration of the skin with hyperkeratotic lesions that can have a proliferative aspect, and class M4.1 as altered skin (M4) with a painful focus (M1).

These different morphological stages can be clearly observed if the feet are lifted in a hoof trimming chute (crush). This method is widely accepted as the reference standard method for diagnosing BDD lesions (Jacobs et al., 2017; Cramer et

al., 2018), but requires significant time and effort. Therefore alternative more rapid BDD examination methods are required. The two most commonly used alternatives are visual assessment in the milking parlour (Thomsen et al., 2008a) or during a pen walk (Jacobs et al., 2017). Of these the former is the most common and has the most variations with some authors just using direct observation (Oliveira et al., 2017b; Yang et al., 2017b) and others using tools such as a mirror (Relun et al., 2011; Solano et al., 2017a), or a borescope (Stokes et al., 2012). The main problem with these rapid BDD detection methods is that compared to lifting the feet they reduce the ability to accurately distinguish between morphological stages; thus amalgamation across categories has to be used to maintain accuracy. For example, Relun et al. (2011) suggested that M3 and M4 should be combined into one category when observing BDD lesions during milking, while Solano et al. (2017a) concluded that the highest degree of agreement was achieved when the simplest classification scheme (presence and absence) was used.

Despite significant resources having been spent on researching BDD, it is a major problem for housed cattle (Capion et al., 2012; Solano et al., 2017b; Jacobs et al., 2018). BDD causes reduced milk production (Relun et al., 2013b), impaired fertility (Gomez et al., 2015), as well as compromising cow welfare issue (Bruijnis et al., 2012) and resulting in significant costs for treatment and control (Cha et al., 2010). Once a herd becomes infected, these costs are likely to be on-going as eradication from a herd is difficult to achieve and the most likely outcome is "manageable control" (Orsel et al., 2018).

Although BDD is commonly considered to be a disease of housed cows (Laven and Lawrence, 2006; Holzhauer et al., 2012), countries with pasture-based systems such as Chile (Rodriguez-Lainz et al., 1998), Australia (Milinovich et al.,

2004) and New Zealand (Vermunt and Hill, 2004) are not free from the disease. In New Zealand, BDD appears to be an emerging disease, having gone from reports of sporadic cases (van Andel et al., 2012) to "presenting on ~ 64% dairy farms" in Taranaki, a region in the North Island of New Zealand within 5 years (Yang et al., 2017b). However, on affected farms, the average cow-level prevalence of lesions was very low at only 1.7% (95%CI: 1.4%-2.1%), with most (53.5%) affected farms having < 3% of cows with observed lesions and the highest within-herd prevalence being only 12.7% found on one farm. In contrast to the variable appearance of the disease in intensive housed cattle in the Northern Hemisphere, the lesions in NZ do not show much variability, with most lesions being small rubbery grey lesions that are present at the top of the interdigital cleft (Yang et al., 2017b). The data from Taranaki taken together with sporadic reports of the disease in cattle in both the South and North Island of New Zealand (van Andel et al., 2012) strongly suggest that BDD is present in the other regions of New Zealand; however we lack information as to how common the disease is at the herd and cow levels.

1.2. Prevalence of BDD

1.2.1. Prevalence measures used

Several prevalence concepts have been used when describing the prevalence of BDD. The first of these is herd-level prevalence, namely the between-herd prevalence, which is based on the proportion of the sampled herds that are affected by BDD, calculated as the number of herds with at least one animal affected/total number of herds in the sample. The second is the within-herd prevalence, which is the proportion of cows affected by BDD in each of the sampled herds, calculated as the number of cows in the herd with lesions/the number of cows examined in the herd

(Yang et al., 2017b). At the cow level, two prevalence measures are used. The first is the overall cow-level prevalence, which is calculated as the number of cows with a lesion/the number of cows examined in either all herds or just herds where BDD has been diagnosed (Holzhauer et al., 2006; Yang et al., 2017b). The second measure is average (median or mean) within-herd prevalence, again this can include or not include uninfected herds (Rodriguez-Lainz et al., 1998; Cramer et al., 2008).

1.2.2. Prevalence of BDD in dairy herds: Current and historical data

In Northern Hemisphere herds, once BDD was introduced, it quickly became established. For example, BDD was first reported in the Netherlands in 1981 (Cornelisse and Peterse, 1981) but around 10 years later a survey by Smits et al. (1992) reported that BDD was very common in herds that used zero grazing. Those authors reported that BDD was detected in 30/34 (88%) herds with lesions observed in 373/2121 (17.6%) cows. Even though all of these herds used a zero-grazing system, in infected herds there was marked between herd variations in the prevalence of BDD, ranging from 1 to 48%. Just over 10 years later, another cross-sectional study, which included both zero-grazed and grazing herds reported that all 47 study herds had BDD and that the median within-herd prevalence of lesions was 24.4% (range 1 to 65%) (Somers et al., 2003). These findings are consistent with a larger cross-sectional study including 383 dairy herds (22454 cows) reported three years later (Holzhauer et al., 2006). Those authors found that 91% of the sampled herds were affected by BDD and lesions were found on 21.2% of cows, with the highest within-herd prevalence being 83%. Recent figures from European and North American countries are consistent with these Dutch data. For example, in Switzerland, Becker et al. (2014) reported that 57/78 herds (73%) were infected and that 29.1% of cows had BDD lesions, while in

Denmark, Oliveira et al. (2017a) reported that 38/39 (97%) Danish herds had BDD with 24.1% of milking cows having BDD lesions, and in Alberta, Canada, 15% cows presented for hoof trimming had BDD and that disease was present on 65/69 (94%) herds where more than 80% cows received routine hoof trimming (Solano et al., 2016).

Most of these data are from housed cows; however as BDD has spread and become endemic on Northern Hemisphere dairy farms, it has also become more common in cattle at pasture. For example while Frankena et al. (1991) reported that they found BDD in 81% of herds and 8.1% of dairy cows at the end of the grazing season, 12 years later Somers et al. (2003) stated that BDD was present at the end of grazing in 49/49 herds and that the median within-herd prevalence of 27.6% (range 2 – 73%).

It is not only the Northern Hemisphere where BDD has become a significant endemic disease. In a survey of Chilean dairy herds Rodriguez-Lainz et al. (1998) reported that BDD was present in 39/43 herds with a median within herd prevalence of 6.1%. Thirty two of those herds were in Southern Chile and most used a combination of grazing and housing. Fifteen years later, BDD had become a significant problem in southern Chile even in herds that were permanently pastured. As part of an ongoing lameness management programme Chesterton (2013) observed BDD in 32/32 pastured herds in southern Chile and concluded that approximately 70% of lameness was associated with BDD.

There are fewer details in regard to BDD prevalence in Australasia. The first large scale study of BDD in that region was undertaken in Taranaki, New Zealand (Yang et al., 2017b). That study found BDD in 143/224 (64%) herds although the mean cow level prevalence was low (1.7%), with most affected farms (53.5%) having

< 3% of cows with observed lesions. The highest within-herd prevalence was only 12.7%. The disease in Australia has shown a quite different prevalence pattern. In 2015, three commercial dairy herds with 185, 180 and 262 cows respectively were screened for BDD in South East Queensland. BDD lesions were found on 139/185 (75.2%) and 94/180 (52%) cows in the first two herds (Avila et al., 2015). Three years later, Coombe et al. (2018) reported that BDD was found in 13/13 dairy herds in Victoria (5490 cows in total), the mean within-herd prevalence was 19.11% (range 6.2 – 32%).

1.2.3. Determining prevalence of BDD

These prevalence estimates are all based simply on visual examination of the feet of individual cows. In many cases this examination has been performed during hoof trimming in a hoof trimming chute (Manske et al., 2002; Somers et al., 2003; Thomsen et al., 2008b), and this form of examination has been considered as the reference test for BDD (Rodriguez-Lainz et al., 1998; Laven, 1999; Jacobs et al., 2017). However, observation in a trimming chute takes a significant amount of time and is not suitable for the repeated routine herd level measurement of BDD prevalence that is recommended to identify early cases of the disease and to make sure DD remains manageable at the herd level (Döpfer and Bonino Morlán, 2008). Thus for routine monitoring and large-scale prevalence studies alternative methods of BDD detection are required. Ever since Rodriguez-Lainz et al. (1998) first used observation during milking as an alternative to BDD inspection in the trimming chute, this method has been widely used in BDD studies (Thomsen et al., 2008a; Relun et al., 2011; Oliveira et al., 2017a; Solano et al., 2017a; Yang et al., 2017b; Cramer et al., 2018).

Several studies have compared observation during milking to observation in a trimming chute (see Table 1). The general conclusion of these studies is that examination in the milking parlour is an adequately reliable method to detect BDD lesions if the aim is to determine BDD prevalence (Relun et al., 2011; Solano et al., 2017a). However, this conclusion ignores the fact that the difference between apparent prevalence (scored in the milking parlour) and true prevalence (scored in the trimming chute) depends on true prevalences. This is illustrated in Table 2 for range of true prevalences from 1 - 60%.

Table 1-1 Apparent prevalence (scored in the milking parlour), true prevalence (scored using trimming chute) and performance for scoring bovine digital dermatitis lesions in the milking parlour, considering scoring in the trimming chute as the reference test.

Study	N	Prev (chute)	Prev (milking)	Specificity	Sensitivity
Rodriguez-Lainz et al. (1998)	117[a]	27%	20.5%	0.99	0.72
Thomsen et al. (2008a)	786[b]	28.8%	29.9%	0.84	0.65
Relun et al. (2011)	484[b]	45%	51.5%	0.8	0.9
Solano et al. (2017a)	6991[b]	57.3%	58.1%	0.876	0.922
Cramer et al. (2018)	1104[b]	44%	28%	0.953	0.577

a: number of cows inspected
b: number of feet inspected

Table 1-2 Computed apparent prevalence based on the pre-defined true prevalence (scored using trimming chute), sensitivity and specificity for scoring bovine digital dermatitis lesions in the milking parlour.

	Thomsen et al. (2008a)[a]	Relun et al. (2011)[b]	Solano et al. (2017a)[c]	Rodriguez-Lainz et al. (1998)[d]	Cramer et al. (2018)[e]
True prevalence	Apparent prevalence				
1%	16.5%	20.7%	13.2%	1.7%	5.2%
5%	18.5%	23.5%	16.4%	4.6%	7.4%
10%	20.9%	27.0%	20.4%	8.1%	10.0%
20%	25.8%	34.0%	28.4%	15.2%	15.3%
30%	30.7%	41.0%	36.3%	22.3%	20.6%
40%	35.6%	48.0%	44.3%	29.4%	25.9%
50%	40.5%	55.0%	52.3%	36.5%	31.2%
60%	45.4%	62.0%	60.3%	43.6%	36.5%

a: sensitivity = 0.65, specificity = 0.84
b: sensitivity = 0.9, specificity = 0.8
c: sensitivity = 0.922, specificity = 0.876
d: sensitivity = 0.72, specificity = 0.99
e: sensitivity = 0.577, specificity = 0.953

It is clear that apparent prevalences can be dramatically biased in many scenarios. For each study the bias that is the difference between apparent prevalence (p) and true prevalence (π) (i.e. $|p-\pi|$) has a minimum around a particular true prevalence level, e.g. ~10% Cramer et al. (2018), ~30% Thomsen et al. (2008a) and ~60% Solano et al. (2017a). Thus whether the bias in using milking parlour rather than chute observation is acceptable depends on specificity, sensitivity and true prevalence. For example, if we define an acceptable apparent prevalence as one that is not k higher or lower than the true prevalence, i.e. $|p-\pi| < k$, where k is an arbitrarily defined percentage. Since $p = \pi\eta + (1-\pi)(1-\theta)$, we know p is acceptable if $\min(\frac{k-\theta+1}{2-\eta-\theta}, 1) > \pi > \max(\frac{k+\theta-1}{\eta+\theta-2}, 0)$, as $\frac{k-\theta+1}{2-\eta-\theta} > 1$, if $k > 1-\eta$ and $\frac{k+\theta-1}{\eta+\theta-2} < 0$, if $k > 1-\theta$, where η and θ are sensitivity and specificity of milking parlour examination (hence, both < 1). The above constraint on π suggests that examination in the milking parlour with particular estimates of sensitivity and specificity is only reliable for study populations with particular range of true prevalences, unless one allows $k > 1-\eta$ and $k > 1-\theta$ at the same time, namely, either the sensitivity and specificity are both extremely high (which is not true) or k is set to be relatively large, e.g. $k \geq 12.4\%$ as per Solano et al. (2017a) which so far has the highest reported sum of sensitivity (0.922) and specificity (0.876). In different populations with distinct true prevalences, it is likely that using milking parlour examination alone can produce unacceptable prevalence estimates, i.e. π does not fall in the defined range. Therefore examination using trimming chute is an essential approach to obtain accurate prevalence estimates, however, if using such facility is not feasible under specific conditions, alternative study design and statistical adjustment are required in order to calculate the true prevalence.

Vink et al., (2009) compared lesion examination in the milking parlour to serological status (based on ELISA test results). True prevalence, sensitivity and specificity were then calculated from lesion status and ELSA test results. However, the true prevalence Vink et al. (2009) calculated was the true prevalence of BDD infection rather than the true prevalence of BDD lesions. Thus the sensitivity they calculated was the probability of detecting a lesion given the animal was truly infected with BDD (Jones et al., 2009). For assessing milking examination against trimming chute examination, the sensitivity that is important is the probability of detecting a lesion given the animal really has a BDD lesion(s). The same distinction can also be applied to the interpretation of specificity. Therefore, if the aim is to estimate the true prevalence of BDD lesion-positive in New Zealand, the design used by Vink et al. (2009) is not optimal.

In the New Zealand situation where few farms have trimming chutes and there is a high cow-to-staff ratio, the only feasible method of detecting BDD lesions is identification during milking. Thus in order to have confidence in the estimates of BDD, we need data on the specificity and sensitivity of BDD lesion detection during milking under New Zealand conditions. However we lack specific New Zealand-based data equivalent to the studies presented in Table 1 that would allow us to directly calculate a New Zealand-specific sensitivity and specificity for foot examination in the milking parlour.

Using data from their survey of lesions in Taranaki (Yang et al., 2017b), Yang et al. (2017a) were able to estimate the true prevalence of BDD lesions in that region of New Zealand by using a Bayesian latent class model and priors for sensitivity and specificity derived from the published evidence summarised in Table 1 combined with New Zealand expert opinion. However, this model used a binomial distribution

and thereby ignored the finite nature of the dairy herds which the sampled animals were drawn from. Sampling without replacement from a finite population is best described using a hypergeometric distribution. The complexity of this distribution has resulted in only a few applications in the veterinary field being found, e.g. Hanson et al. (2003) who used hypergeometric sampling to determine the infection status of a herd and Su et al. (2004) who used the same approach to infer the total number of infected animals in a finite population.

The difficulty in using the hypergeometric distribution led to the development of the Bayesian superpopulation approach, which uses ideas from the sample survey literature on Bayesian finite population inference (Jones and Johnson, 2016). This approach is a great alternative to the hypergeometric approach when making inference for finite populations, such as dairy herds, since it uses a modified binomial method which is much simpler than the hypergeometric method. The basic idea of the Bayesian superpopulation approach is to assume that a real finite population can be seen as a random sample from an imaginary superpopulation. As the superpopulation is infinite, we can make an inference for the superpopulation using the binomial model. This inference for the superpopulation can then be used to make an inference back to the unsampled portion of the finite population.

To estimate disease prevalence in dairy cattle, a two-stage sampling scheme is required, i.e. a number of herds are selected from the population of herds, and then, within each sampled herd, a number of animals are sampled. From the Bayesian superpopulation perspective, a number of superpopulations can be assumed to be sampled independently from the population of the superpopulations and hence each finite dairy herd can be regarded as a random sample drawn from its own

superpopulation. This then allows prevalence estimates to be made using data from the finite herds without using a statistical method whose assumptions are violated.

Using Bayesian superpopulation framework for diagnostic test outcome data is a new idea, and so far few applications have been published. Jones and Johnson (2016) re-analysed three datasets using their approach, one of which will be briefly discussed as an example (Hanson et al., 2003). Those authors applied a screening test for *M. a. Paratuberculosis* infection to a dairy herd of 493 animals using an imperfect ELISA test with pre-defined cut-off points. Six animals returned positive results. The question that Hanson et al. (2003) were interested in was the probability of the herd being infected. So let p_I denote the probability that the herd is infected. Using the superpopulation approach, Jones and Johnson (2016) reported that the probability of the herd being infected was 0.02 which was in consistent with reported by Hanson et al. (2003), although a distinction was noted that superpopulation model required 40 or more test positives to give a probability of infection above 0.9, whereas Hanson et al. (2003) suggested that was 38.

The superpopulation approach can be generalised to model one test on multiple populations with a hierarchical population structure and is therefore the model of choice to estimate the herd and animal level prevalence of BDD in New Zealand.

1.3. Risk factors

1.3.1. Cow-level risk factors

Multiple studies across many different countries have investigated the factors at the cow level which could increase the risk of an animal having BDD. Most of these studies have focused on the presence/absence of BDD lesions.

1.3.1.1. Breed

Multiple studies have shown that Holstein-Friesian cattle have a significantly higher risk of BDD than other breeds. For example, in one of the earliest studies evaluating BDD risk factors, Frankena et al. (1991) found that on Dutch dairy farms, cows with more than 50% Holstein-Friesian genetics had a higher risk than other breeds. This breed effect was still present in the Netherlands 15 years later; Holzhauer et al. (2006) reported that Holstein-Friesians or their cross-breeds had a greater risk of having BDD lesions than Meuse-Rhine-Issel cattle breed. Similar results have been reported in many other countries including France (Relun et al., 2013a) and Chile (Rodriguez-Lainz et al., 1999).

1.3.1.2. Parity and age

Many studies have found that risk of BDD declines with increasing parity (Rodriguez-Lainz et al., 1999; Somers et al., 2005; Holzhauer et al., 2006). Figure 1 summarises the findings reported by these studies. Several reasons for this age effect on BDD lesion prevalence have been suggested. Firstly, young animals may be more likely to have BDD due to the stress associated with environmental changes during calving, especially mixing with the older cows (Holzhauer et al., 2006). Secondly, immunity to BDD appears to increase with age, with older cows appearing to be more resistant to developing lesions after exposure to BDD-related bacteria (Blowey et al., 1994; Read and Walker, 1998). Thirdly, younger animals have lower heels (Vermunt and Greenough, 1995), therefore they may be more likely to develop BDD lesions because of the increasing contact between the area of skin that is typically affected by BDD and the slurry which probably contains the bacteria responsible for BDD (Laven, 2007). Finally, increased culling of older cows with BDD may be a management-

related reason for older cows having a lower prevalence of BDD (Rodriguez-Lainz et al., 1999).

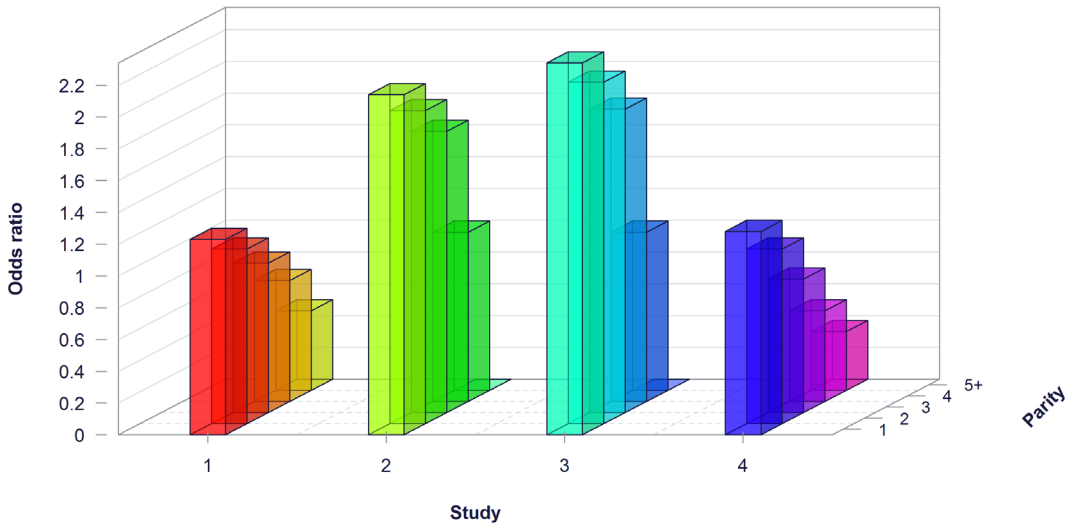

Figure 1-1 A summary of effects of parity on bovine digital dermatitis from the four studies; 1: Holzhauer et al. (2006), 2: pasture period as per Somers et al. (2005), 3: housing period as per Somers et al. (2005), 4: Rodriguez-Lainz et al. (1999).

Not all studies have shown that BDD is highest in first parity; Argáez-Rodríguez et al. (1997) reported that cows in their second parity 102/215 (47%) were at higher risk of having observable lesions of BDD compared to other parities (1/92 (1%) at parity 1, 40/127 (31%) at parity 3, 34/101 (34%) at parity 4 and 8/33 (24%) at parity 5). Palmer and O'Connell (2015) suggested that differences between studies in the parity with the highest risk of BDD could, at least in part, be due to keeping heifers separate from the main dairy herd until they calved for the second time. Stresses such as mixing with the older cows would therefore be delayed start of the second lactation.

1.3.1.3. Stage of lactation

Although there is a general agreement that lactating cows have a higher risk of BDD than dry cows (Argáez-Rodríguez et al., 1997; Holzhauer et al., 2006; Holzhauer et al., 2008b), it is unclear at which stage of lactation cows are most likely to develop BDD. Argáez-Rodríguez et al. (1997) reported the highest risk of BDD (9%) in the first month after calving. In contrast in the Netherlands, BDD prevalence in the first month after calving was not significantly different from that reported more than 60 days in milk (Holzhauer et al., 2006). Instead, those authors found that for third parity cows only, at peak lactation (30 to 60 days in milk) the odds of BDD were increased compared to >60 days in milk (OR: 1.4, 95%CI: 1.1-1.8). This finding was consistent with a previous Dutch study that reported that cows at 30 to 70 days in milk had the highest risk for BDD (Frankena et al., 1991). These inconsistencies between Mexican and Dutch findings may be related to differences in climate. In Mexico, the summer temperature is over 40°C and during winter there is very little rainfall; while in the Netherlands, the summer temperature is 17°C-20°C, and rainfall is distributed throughout the year with a dryer period from April to September which is the spring and summer. Nevertheless, although there may be small differences in timing of peak prevalence of BDD, it is clear that most cases of BDD cases occur within 100 days of calving (Capion et al., 2009).

1.3.2. Farm-level risk factors

Multiple studies have identified a large number of farm-level risk factors which affect BDD prevalence including access to pasture (Holzhauer et al., 2012); housing type (straw yards vs. cubicles and tractor vs. automatic scraping) (Laven, 1999); cleanliness of cows' legs (Relun et al., 2013a); cattle purchasing policy

(especially of heifers) (Rodriguez-Lainz et al., 1999); and the use of hoof trimmers who work on multiple farms and cleaning of hoof trimming equipment (Wells et al., 1999).

At the farm-level, risk factors can have two effects. Firstly they can influence whether a disease is present on a farm and, secondly, if a disease is present on a farm they can influence within-farm prevalence. As far as the author is aware none of the previous papers on risk factors for BDD have separated these two effects, with the principal outcome of previously published studies being primarily the probability of a cow having BDD lesions, rather than the probability of a herd having any affected cows. For example, two Dutch studies investigated both cow- and farm-level risk factors for BDD at the same time, but in both cases the outcome variable was measured at the cow rather than the farm level (Somers et al., 2005; Holzhauer et al., 2006). In contrast, Rodriguez-Lainz et al. (1999) used separate models to study farm- and cow-level risk factors for BDD, but their outcome variable was still just within-farm prevalence. One notable exception was the study by Wells et al. (1999). That study used a dichotomous outcome at the farm-level based on whether a farm was above or below a 5% threshold prevalence of BDD lesions. This is similar to the process needed to analyse the impact of risk factors on presence/absence of BDD lesions. Nevertheless, as both of these categories included herds with BDD, the study by Wells et al. (1999) still only provided evidence as to whether a risk factor altered within-herd prevalence of BDD rather than whether it altered the probability of BDD lesions being present on a farm. This lack of focus in European and North American studies on within-herd prevalence rather than herd-level prevalence is probably because of very high herd-level prevalence of BDD on dairy farms in Europe and North America (Holzhauer et al., 2006; Solano et al., 2016). In contrast in New

Zealand, although initial studies suggested that herd level prevalence (~60%) was higher than expected it was lower than that reported in Europe and North America (Yang et al., 2017b), and at a level where understanding risk factors that were associated with BDD absence at the farm level could be useful in developing strategies to keep farms free of BDD.

1.3.3. Analytical models

To investigate risk factors which could influence both whether a farm has BDD lesions and the prevalence of BDD on affected farms, either hurdle or zero-inflated models are required (Neelon et al., 2016).

Hurdle models are comprised of a point mass at zero and a zero-truncated count distribution for the positive cases. Hurdle models thus generate two models: a logistic regression model (for the zero 'effect') and a Poisson or negative binomial (NB) model, depending on dispersion (for the count 'effect'). The logistic regression model thus predicts the likelihood of at least one cow with BDD lesion(s) being present on the farm, while the Poisson or NB model is used to predict the number of cows with BDD lesions (>0). Thus for Poisson hurdle model (PH) we have:

$$P(Y_i = y_i|p_i) = 1 - p_i, if\ y_i = 0$$

$$P(Y_i = y_i|\lambda_i, p_i) = p_i \frac{{\lambda_i}^{y_i} e^{-\lambda_i}}{y_i!\,(1 - e^{-\lambda_i})}, if\ y_i = 1,2,3\ \ldots$$

where p_i is the probability that BDD lesions are present on a farm and λ_i is the Poisson mean.

To study farm-level risk factors, the model with covariates can be then extended: $\text{logit}(p_i) = \gamma X_i$ and $\ln(\lambda_i) = \ln(N_i) + \beta X_i$, where γ is a vector of logistic regression coefficients, β is a vector of regression coefficients of the Poisson model and X_i is a vector of predictors such as farm management practices. N_i is the herd size

of i^{th} farm, hence $\ln(N_i)$ is an offset term which accounts for the effect of herd size on the number of BDD lesions in a herd (more cows means more lesions assuming probability of a lesion at the individual level stays the same under the same management in a herd), and therefore allows the Poisson model to predict the proportion of cows with BDD lesions in a herd.

In contrast to hurdle models, zero-inflated models are comprised of a degenerate distribution at zero and a count distribution (Poisson or NB) for the positive cases. Thus in the zero-inflated models, zeros come from two sources since zeros can arise from the Poisson or NB distribution as well as the degenerate distribution. Thus, for zero-inflated Poisson model (ZIP) we have:

$$P(Y_i = y_i|\lambda_i, p_i) = 1 - p_i + p_i e^{-\lambda_i}, if\ y_i = 0$$

$$P(Y_i = y_i|\lambda_i, p_i) = p_i \frac{{\lambda_i}^{y_i} e^{-\lambda_i}}{y_i!}, if\ y_i = 1,2,3 \ldots$$

As with the hurdle models, the logarithm of the number of herd size is added as an offset to the Poisson or NB model so that that model predicts the prevalence instead of the counts. Adding covariates, the models can be extended $\text{logit}(p_i) = \gamma X_i$ and $\ln(\lambda_i) = \ln(N_i) + \beta X_i$.

If the overdispersion is suspected, a NB distribution can be used for zero-inflated or hurdle models rather than a Poisson distribution. Both negative binomial hurdle model (NBH) and zero-inflated negative binomial model (ZINB) models are expressed as:

NBH

$$P(Y_i = y_i|p_i) = 1 - p_i, if\ y_i = 0$$

$$P(Y_i = y_i|\pi_i, r, p_i) = p_i \binom{y_i + r - 1}{y_i} \frac{{\pi_i}^r (1 - \pi_i)^{y_i}}{1 - {\pi_i}^r}, if\ y_i = 1,2,3 \ldots$$

ZINB

$$P(Y_i = y_i|\pi_i, r, p_i) = 1 - p_i + p_i{\pi_i}^r, if\ y_i = 0$$

$$P(Y_i = y_i|\pi_i, r, p_i) = p_i \binom{y_i + r - 1}{y_i} {\pi_i}^r (1 - \pi_i)^{y_i}, if\ y_i = 1,2,3 \ldots$$

where $\pi_i = \frac{r}{r+\lambda_i}$, and r is the inverse dispersion parameter. In the regression setting, ZINB and NBH have the same form as ZIP and PH.

The selection of the hurdle or zero-inflated models is often based on information-theoretic selection measures such as Akaike information criterion (AIC) (Akaike, 1974), the small-sample "corrected" AIC (AICc) (Sugiura, 1978), and the Bayesian information criterion (BIC) (Schwarz, 1978), a model with a smaller value of the criterion being is considered superior to the competing one. "Being smaller" usually means, for example, a difference of 10 or more in AIC between two competing models (Burnham and Anderson, 2004).

However, this selection process ignores the biology of BDD which also needs to be considered. The binary response variable modelled by the logistic regression in zero-inflated models is not observed; hence the model can be seen as a latent class model where the zero arises from two processes (Neelon et al., 2016). Therefore, p_i is not the probability that observable lesions are present on a farm. In epidemiology, this probability p_i is known as "at-risk" probability (Preisser et al., 2012; Albert et al., 2014). For example, for BDD defining a farm as being at risk (of having BDD lesions) does not mean that cows with BDD lesions have been observed on the farm, as BDD seropositive cows do not always have clinical lesions (Vink et al., 2009).

This means that if the outcome of interest is presence or absence of observed lesions at the farm level rather than whether farms are at risk of having them, then zero-inflated models are not appropriate. In contrast, the binary response in a hurdle

model is based on whether the observed count response (number of cows with lesions) is non-zero and does provide a measure of the probability that observable lesions are present on a farm. As in New Zealand, the presence/absence of BDD lesions at the herd level is a primary focus of this research rather than whether farms are "at risk" of having BDD; hurdle models better match the rationale behind the analysis.

So far, all the discussions in this section has assumed that the diagnostic method used is perfect, i.e. animals with BDD lesions are not missed and that animals reported as having BDD lesions actually have BDD lesions. However, visual inspection in the milking parlour for BDD lesions, which is the best method for large scale BDD diagnosis on New Zealand farms, is an imperfect diagnostic method (Thomsen et al., 2008a). Therefore, any analysis of data from such detection, even if it is focused at the herd level, must take into account that not all lesions identified as BDD will be BDD lesions and not all cow identified as not having BDD will truly not have BDD. Thus, apparently BDD-free farms may still have a low within-farm prevalence of BDD lesions, and farms with a low number of apparent BDD lesions may actually be BDD-free. If a simple dichotomised approach is used, based on whether or not there is at least one cow with "BDD" lesion(s) found on the farm, then information regarding the likelihood of the categorisation being correct is lost; for example a herd with 40 detected lesions is treated as being the same as a herd with only one detected lesion.

To overcome this problem, a Bayesian latent class model can be used to predict the probability of a farm having BDD lesions conditional on the number of animals with detected lesions, the total number of animals tested on each farm and the test sensitivity and specificity (Yang et al., 2017a). Then, rather than a simple dichotomised presence/absence, predicted probability can be used as the response

variable, and its relationship with the farm management practices modelled using a beta regression model under the Bayesian paradigm (McAloon et al., 2017). The Bayesian beta regression model can be combined with the Bayesian superpopulation approach (introduced in the previous section) and if farms are sampled from more than one region, the beta model can be extended into the multilevel setting.

1.4. Transmission dynamic of BDD

In appearance, BDD is a very variable disease (Plummer and Krull, 2017). These changes in appearance are linked to the clinical progress of the disease and several scoring systems have been proposed to describe the different appearance of BDD lesions at each stage. These include the colour score system (Laven, 1999), M-score system (Döpfer et al., 1997; Berry et al., 2012) and Iowa DD scoring system (Krull et al., 2014). The main aim of identifying these different stages is to understand the dynamics of BDD in a population (through understanding lesion transition) and thereby develop intervention and treatment strategies (Döpfer et al., 2012).

In order to develop these strategies, modelling of BDD, especially of the lesion transitions is essential, and several authors have published their models of lesion transitions, including Döpfer et al. (2012) and Biemans et al. (2018) who built models using the M-score system and Krull et al. (2016) who proposed a model based on the Iowa DD scoring system.

The model developed by Döpfer et al. (2012) was based on data from a study by Holzhauer et al. (2008b). Animals were allocated into five groups with different footbathing strategies (Holzhauer et al., 2008a). All the animals were examined for BDD lesions and scored using the M-score system every 3 weeks by the

herd manager. In total, there were eight examinations per cow between Jan and Jun 2004. Topical chlortetracycline spray was applied to all BDD lesions at detection. The model structure was constructed according to the original five M-scores (M0 – M4) (Döpfer et al., 1997); M4.1 was not included in the model. The authors assumed there was one susceptible (S) class (M0), two infectious (I) classes (M2 and M4), and two latently infected (infected but not infectious; E) classes (M1 and M3). The compartmental model used by Döpfer et al. (2012) thus adopted the SEIS structure to model the infection dynamic (M-score transitions) in a large closed population. Transitions between the lesion stages as observed in the field were adopted by the model. Table 3 summarises the transitions and restrictions of movements between different lesion stages as per Döpfer et al. (2012).

Table 1-3 Transitions between bovine digital dermatitis lesion stages observed in the field and adopted by the model as per Döpfer et al. (2012).

From	To
M0	M1 and M4
M1	M0, M2, M3 and M4
M2	M1, M3 and M4
M3	M1, M2 and M4
M4	M0, M1, M2 and M3

Döpfer et al. (2012) reported lesion transition rates for the five different footbath groups, alongside estimates of the infectiousness of M2 and M4 lesions and the basic reproduction ratios. The mean estimates for the infectiousness of M2 were larger than the infectiousness of M4 in 3 out of 5 groups (e.g. 0.68 vs 0.15 for group 5) indicating that M2 lesions contribute more to the force of infection compared to M4 lesions in most of the groups. No significant differences in basic reproduction ratio were found between the footbaths groups consistent with the findings of Holzhauer et al. (2008b) who had analysed the data using a simpler logistic regression model. Döpfer et al. (2012) assumed that there was only one transition between M-scores in

the time interval between two lesion examinations. Thus this model is dependent on the examination interval being sufficiently short for this assumption to be correct. A three week interval was adopted in this study, but the optimal time interval is likely to be dependent on the persistence of BDD in the particular dairy system under consideration.

The second modelling study which adopted the M-scoring system was undertaken by Biemans et al. (2018). However, they used a different model structure. In contrast to Döpfer et al. (2012) who considered only M2 and M4 to be infectious and constructed an SEIS model, Biemans et al. (2018) treated all BDD lesions (i.e. M1, M2, M3, M4 and M4.1) as different infectious classes with different levels of infectiousness and constructed an SIS model. The main aim of the modelling undertaken by Biemans et al. (2018) was to study the differences in infectiousness between different M-stages, the persistence (sojourn time) within each stage and the contribution of each M-stage to the basic reproduction ratio. The analysis was performed using data was collected on 12 Dutch dairy farms between Nov 2014 to Apr 2015, with the farms being visited fortnightly for a total of 11 examinations. In contrast to Döpfer et al. (2012) who treated all BDD lesions on detection, Biemans et al. (2018) did not treat cases or inform farmers of their findings. Nevertheless, farmers were able continue their normal BDD control and treatment programme.

Biemans et al. (2018) concluded that the majority of the lesions transitions were from M0 to M4 (93.89%) and that all the other lesion stages rapidly transitioned to M4, resulting in approximately 70% of the infectious duration being in M4. The transmission rates, i.e. the product of the contact rate between animals and the probability of the contact leading to infection of M1 (0.016), M2 (0.039), M3 (0.040), and M4 (0.042) were not significantly different from each other but were all much

lower than that of M4.1 (0.322). Nevertheless, even though the transmission rate of M4 was not the highest M4 lesions made the greatest contribution to the basic reproduction ratio (89%) as i) most BDD cases were first observed as M4 and ii) because of the relatively long sojourn time in M4 compared to the other M-stages. Biemans et al. (2018) concluded that preventing the development of the M4-stage was crucial if the incidence of BDD was to be decreased on a farm.

These two studies show that modelling using the M-score system can be useful in dairy systems where BDD has been present for over 30 years and has become endemic in the dairy cattle population. However, it may not capture the disease infection dynamic in the pasture-based dairy system in New Zealand. There are several reasons for this. Firstly, BDD has probably not been present in New Zealand for the same length of time that it has in the Northern Hemisphere, being first identified in 2004 (Vermunt and Hill, 2004). This, combined with the pasture-based nature of dairying in New Zealand, has meant that the current prevalence of BDD (~2 in infected herds) is very low (Yang et al., 2017b). In addition to low prevalence, lesion persistence appears to be short and the consequence of BDD lesions are generally limited with little clinical lameness being observed in affected cattle (Yang et al., 2017b). This lack of impact has meant that treatment of BDD is very rare and the use of preventative programmes such as routine footbathing even rarer. It is likely that the lesion transition process will be different in the absence of treatment, for example the M3 stage is often described as the post treatment stage (Berry et al., 2012), and has not been reported in New Zealand. Indeed BDD in New Zealand is much less variable than BDD in the Northern Hemisphere, with the great majority of lesions being small rubbery M4-like lesions and M2-like active lesions being extremely rare.

This analysis suggests that M-scoring system may not be ideal for describing BDD-transitions in New Zealand. A scoring system that may be more applicable is that developed by Krull et al. (2014). They developed the Iowa DD scoring system after finding that the M-scoring system could not fully describe the early stage lesions of BDD that they observed. The scoring system has five stages: normal skin (stage 0), lesion onset (stage 1 with sub-classes type A and B), developing lesions (stage 2), classical ulceration (stage 3), and chronic lesions (stage 4) (Krull et al., 2014). Krull et al. (2016) used this scoring system to observe BDD lesion progression and regression over 3 years without any standard BDD treatment or preventative procedures. They proposed that all severe BDD lesions began with early lesions (stage 1 or stage 2). However, not all early lesions eventually became severe lesions; some early lesions persisted without changing grossly, while others regressed and became normal. As the Iowan stage A1 lesion in Iowa is very similar grossly to the small rubbery M4-like lesion that is most commonly observed in New Zealand, this scoring scheme may suit the New Zealand system better than the M-score. However, as severe lesions (stage 3 and stage 4) are rare in New Zealand and lack of routine treatment means that regressing lesions are also uncommon, the Iowa system cannot be simply applied directly to model the BDD infection dynamic in New Zealand, but needs modifying and testing using New Zealand-specific longitudinal data.

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Chapter 2. Farm Level Risk Factors for Bovine Digital Dermatitis in Taranaki, New Zealand: An Analysis Using a Bayesian Hurdle Model

This chapter is prepared in the style format of The Veterinary Journal. The published manuscript is presented in appendix.

2.1. Abstract

As part of a cross-sectional study of bovine digital dermatitis (BDD) in 60455 cows across 224 herds in Taranaki region of the North Island of New Zealand, questionnaire based interviews were also undertaken in order to identify the key management practices which affect the probability of a farm being infected with BDD, and, on infected farms, the prevalence of an individual cow being affected. The data from the questionnaire were analysed using a Bayesian hurdle model (i.e. a model with two stages; the first of which modelled the odds of a herd being positive, and the second, the prevalence of BDD within an infected herd).

Two factors were identified as being associated with farm level infection status: 1) milking parlour type as farms which had rotary platforms were more likely to be recorded as having BDD than those which had a herringbone (odds ratio [OR]: 3.19, 95% probability interval [PI]: 1.31, 8.51), and 2) young stock movement, with farms whose young stock were reared on farms alongside heifers from other farms having a higher odds of being BDD positive than farms where heifers were kept separate (OR: 4.15, 95%PI: 1.39, 15.27). Two factors were found which increased the prevalence of BDD within infected farms: 1) Farms which used outside staff to trim feet had 3.13 times more (95%PI: 1.25, 7.29) than those which did not, while farms examined in spring (September to November) had 2.16 times (95%PI: 1.05, 4.43) more than farms examined in summer (December to February).

2.2. Keywords

Bovine Digital Dermatitis; Risk Factors; Bayesian; Hurdle Model; New Zealand

2.3. Introduction

Bovine digital dermatitis (BDD) was first reported in Italy and since then has spread across the world to become the most important infectious cause of lameness in dairy cattle (Tremblay et al., 2016). Many factors have been associated with risk of BDD. Risk factors at the cow level include parity, lactation stage, production performance and breed (Rodriguez-Lainz et al., 1999; Somers et al., 2005; Holzhauer et al., 2006; Palmer and O'Connell, 2015), while at the herd level risk factors include housing system (Onyiro et al., 2008), biosecurity such as using outside staff to do hoof trimming (Sullivan et al., 2014) and buying replacement animals (Rodriguez-Lainz et al., 1999), diet (Gomez et al., 2014), hygiene (Relun et al., 2013), pasture access (Holzhauer et al., 2012), herd size (Wells et al., 1999), and footbath regimen (Speijers et al., 2010).

In New Zealand (NZ), the first case of BDD was reported in 2004 (Vermunt and Hill, 2004); this was followed by sporadic reports of disease until 2012 when five cases were reported (van Andel et al., 2012). In response to concerns that this might reflect an increase in the disease in NZ, combined with a lack of any information on BDD prevalence in dairy cows in NZ, a pilot study focused on a specific region in New Zealand (Taranaki in the North Island of NZ) was undertaken (Yang et al., 2017). It is likely that risk factors for BDD in New Zealand are similar to those reported elsewhere, but the relative importance of risk factors may differ. For example, the pasture-based nature of dairy farming in New Zealand means that on most farms housing is not a significant risk factor. A survey undertaken in 2015 found that only 4% of dairy farms in New Zealand housed their cows for any period of time. Most of these cows were loose housed with only 0.4% of farms using cubicle (free-stall) housing (H. Thoday, personal communication), which has been most strongly

associated with BDD compared to straw yards or at pasture (Onyiro et al., 2008). The relative importance of other herd level risk factors, such as biosecurity may also be influenced by NZ-specific factors such as the common practice of grazing groups of heifers from multiple farms on a single farm. Thus, alongside the prevalence survey, data were collected at the herd level in order to identify, on pasture-based farms the key risk factors which influenced whether a farm had BDD and, if it did, the prevalence of BDD within that farm.

2.4. Materials and Methods

2.4.1. Study design and data collection

The study design and methodology were previously described by Yang et al. (2017). Briefly, a trained technician visited 224 farms in Taranaki on the North Island of New Zealand between September 2014 and February 2015, and during milking visually inspected every cow for BDD. At the same time a questionnaire (see Appendix 1: Supplementary material 1) was given to the farm owners or manager of every farm inspected. The questionnaire was designed by RNC with input from WDV and RL, based on their experience with BDD and the published literature. Once developed, the questionnaire was tested with six clients of Energy Vets Taranaki Ltd to identify any questions that were unclear before it was used in the main study. Along with the questionnaire, a letter of appreciation and a bag of chocolate were provided to encourage response. A prepaid envelope was attached with the questionnaire for return by post. The management variables collected via the questionnaire are shown in Table 1.

Prior to data analysis, the responses were examined by one of the authors (RNC), in order to identify missing and incorrect records. For seven questionnaires

RNC rang the farmers to complete or adjust the answer the farmers had written. In four of those, the farmers indicated outside staff, i.e. veterinarians, had come to treat the lame cows but had not filled in the % treated by the farmers or veterinarians. In three cases the farmers had written the actual number of cows treated by the farmer and the vet instead of the % treated by each.

2.4.2. Statistical methods

The data were analysed with a Bayesian negative binomial hurdle model. This was a two stage process with the first stage being a binary model that assessed whether or not a farm was infected (i.e. whether it had 0 or ≥1 cases) and the second stage being a zero-truncated negative binomial model which estimated the number of cases on infected farms (Neelon et al., 2016). The two stages were run simultaneously. The outcome of the negative binomial portion of the Bayesian hurdle model (number of cows with digital dermatitis) was converted to the proportion of cows with BDD in a herd (prevalence) by adding the natural logarithm of the number of examined cows in each herd as "an offset" to the model.

The continuous predictors were checked using histograms to see if they were normally distributed. For categorical variables, frequency of occurrence of each category within a variable was identified using one way tables. Categories with low frequencies were combined with adjacent categories if this was biologically plausible (Dohoo et al., 2003a). For example, farmers reported purchasing cows either from farms and sale yards; but the great majority purchased cows from other farms only. This variable was therefore re-categorised as a dichotomous variable describing whether or not cows were purchased. Only variables with substantial variability (at

least two categories per variable with frequency ≥20%) were selected for further analysis.

The predictors included in the multivariable model were determined using a non-Bayesian univariable negative binomial model. All predictors with $P \leq 0.2$ were then included in the multivariable negative binomial model, provided there was no collinearity. For animal purchase, collinearity meant that only the categorical variable of purchase yes or no was used. Firstly, source was only recorded when there was purchase, and secondly number of animals purchased was strongly associated with herd size and proportion of herd purchased had only limited variability. Variables were dropped from the multivariable model using a process of backward elimination with the variable with the highest P-value being removed, until all remaining variables were significant at $P \leq 0.05$. A variable was considered a confounder if coefficients or standard errors of remaining variables altered by ≥15%; confounders were retained in the model even if not significant.

Once this elimination process was finalised, variables which, based on previous studies were thought to be biologically important but were not included in the final model, either because their associated P-value in the univariable model was >0.20, or which were eliminated during the model building stage were added back in the model, one at time (Dohoo et al., 2003a). Those variables were removed from the multivariable model if their P-values were <0.05. Once this process was finished, two-way interactions between all the predictors remaining in the model in the preliminary main effect model were created (Dohoo et al., 2003a), and the backwards elimination process repeated. The exploratory data analysis and the non-Bayesian model building process were performed in Stata 13 (StataCorp, USA)

Once the model was finalised, a Bayesian approach was used to estimate model outputs. Details of the Bayesian negative binomial hurdle model are provided (see Appendix 1: Supplementary material 2). Model fit was evaluated by dividing each of the conditional predictive ordinates (CPO) by the largest CPO and confirming that the majority of scaled CPOs were greater than 0.01 (Congdon, 2005). This was followed by plotting the predicted data against the observed data (Dohoo et al., 2003b).

The model was created using OpenBUGS (see Appendix 1: Supplementary material 3) (Spiegelhalter et al., 2007). Without explicit prior knowledge, we set diffuse, normally distributed priors with a mean of 0 and precision (1/variance) of 0.1 for each of the regression coefficients and natural logarithm of r (the inverse of the dispersion parameter). To assess the sensitivity of the dataset to the choice of priors we ran two sensitivity analyses scenarios by increasing and decreasing the precisions of the regression coefficients by 50% (0.15 and 0.05). For all models, the chains were thinned by five to reduce auto-correlation and then run for 50,000 iterations, after discarding a burn-in period of 5,000. The history and auto-correlation plots were used to assess the model convergence.

2.5. Results

The farm, cow and foot level prevalences of BDD, based on the observational data were reported in Yang et al. (2017). Briefly, 143/224 (64%) farms had at least one BDD infected cattle; within the infected farms, cow level prevalence was 1.7% (95% confidence interval [CI]: 1.4, 2.1%). Questionnaires were delivered to 224 farms and responses were received from 124. After deleting missing values, 114 questionnaires were suitable for this analysis (a response rate of 51%) Of these 114

farms, 71 (62%) had been diagnosed as having BDD. This was not significantly different from the herd level prevalence of the 110 farms (72/110 [65%]) which did not send a useable questionnaire ($\chi^2 = 0.244$; $P = 0.62$).

Five predictors remained in the multivariable model at the end of the modelling process (Table 2). All the variables were categorical variables and no statistically significant interactions were found. There was no evidence of lack of convergence or strong auto-correlation in the model. The model had a good fit as 97.4% of scaled CPOs were >0.01. The dispersion parameter from the negative binomial hurdle model was 1.82 and its 2.5% quantile (0.77) was >0, confirming overdispersion and validating the use of a negative binomial model rather than a Poisson. The model's predictive ability is presented in Figure 1.

The risk factors found to have an effect on the risk of BDD at the farm level were young stock movement (odds ratio [OR]: 4.15, 95% probability interval [PI]: 1.39, 15.27) and parlour type; compared to herring bone parlours, farms with rotary parlours were more likely to be reported as being positive (OR: 3.19, 95%PI: 1.31, 8.51) Within infected farms using external staff for hoof trimming increased the proportion of affected cows detected on positive farms (prevalence ratio [PR]: 3.13, 95%PI: 1.25, 7.29). Although farm level prevalence was not affected by season, more affected cows were found on infected farms in spring than summer (PR: 2.16, 95%PI: 1.05, 4.43).

The sensitivity analysis showed that the negative binomial hurdle model was, overall, reasonably robust, particularly for the outputs related to within farm infection. The posterior medians identified as statistically important (see Table 3) changed by up to 5.3% as a result of changing the precision of the regression coefficients, while the statistically unimportant posteriors changed by up to 19.2% (Table 4). When the

precision of the priors increased, the posterior medians tended towards zero; when the precision of the priors decreased, the posterior medians tended to infinity. This suggested that more diffuse priors resulted in stronger effects for the significant associations and vice-versa.

2.6. Discussion

This study identified two factors which influenced the odds of a farm being identified as having BDD -- young stock movements and parlour type, while, on infected farms, season of inspection and whether outside staff trimmed hooves were associated with BDD prevalence.

The association between management of heifer rearing (i.e. kept on farms with other young stock or not) is a New Zealand-- specific finding. Nevertheless, it is consistent with data from elsewhere that buying replacement heifers from other farms can increase the risk of BDD being present on a farm and prevalence within a farm (Rodríguez-Lainz et al., 1996; Rodriguez-Lainz et al., 1999; Wells et al., 1999). This suggests that exposure to heifers from other herds increases the risk of heifers becoming infected and bringing in BDD to a previously uninfected herd; highlighting the potential importance of heifers as a reservoir for BDD (Laven and Logue, 2007; Gomez et al., 2015). Nonetheless, unlike Rodriguez-Lainz et al. (1999) and Wells et al. (1999), no effect of heifer exposure to other herds was found on prevalence of BDD within infected herds, perhaps because the level of infection within infected herds was so low (average 1.7%; Yang et al., 2017) that cow-cow transmission was very rare. No effect of purchasing adult cattle was found on the odds of a herd being infected or on prevalence within an infected herd. This is consistent with overseas studies (Rodriguez-Lainz et al., 1999; Somers et al., 2005) and may be related to the

relative number of cows purchased. Purchasing large number of adult cows is less common compared to buying heifers as replacement animals.

The other factor that was associated with a farm's odds of being BDD positive was the type of milking parlour, with farms with rotary platforms being more likely to be identified as BDD-positive than those with herringbone parlours. Rather than actual herd prevalence, this may reflect the ease of observing small BDD lesions on a rotary platform, especially in herds where there is a low prevalence of BDD. Further research is required to test this finding.

In this study the use of outside hoof trimmers was associated with an increased prevalence of BDD. This effect was also reported by Wells et al. (1999), who found that herds which used outside staff were 2.8 times more likely to have a BDD prevalence of >5% than herds which did not. Wells et al. (1999) stated that their finding could be an effect of increased BDD rather than a cause; however, in our case this would not be so as BDD was extremely rarely associated with lameness so would not have been a reason for the use of outside staff. It is likely that this increased risk is due to failure to clean equipment properly between cows and, especially between farms, as the treponemes associated with BDD can be found on hoof trimming equipment even after a short disinfection process (Sullivan et al., 2014). It remains unclear why the effect is on prevalence within infected herds as there would not appear to be any difference between the chances of poor disinfection spreading disease if the knife belongs to a member of the farm staff or to an outside trimmer.

Although farm level prevalence did not change with season, a higher prevalence of BDD was seen on infected farms in spring than in summer. This might have been associated with the increased rainfall seen in spring, as moist underfoot conditions have been associated with increased BDD (Laven and Logue, 2007;

Gomez et al., 2012), however, the seasonal nature of dairying in New Zealand means that the difference in prevalence between spring and summer could also have been due to the increased stresses associated with calving and the onset of lactation (Capion et al. (2008) reported in non-seasonally calving cows that peak prevalence of BDD occurred within 3 months of calving), as well as the mixing of possibly naïve heifers and infected older cattle. However, these suggestions need further evaluation as this was a cross-sectional study, so the difference in prevalence between seasons was confounded by farm.

This study was a study of farms serviced by one veterinary practice in Taranaki; as such it may not reflect risk factors across New Zealand, especially if there are significant differences between regions in the prevalence of BDD. Further research is required to establish whether these findings are consistent across New Zealand and establish the key risk factors for BDD in cows kept at pasture.

2.7. Conclusions

This study identified four risk factors associated with BDD prevalence (at the herd level or within infected farms) in the Taranaki region: young stock management, parlour type, use of outside staff for foot trimming and season. Of these four factors, the effect of parlour type may reflect ease of diagnosis rather than being a true risk factor, while seasonality may be a chance finding as it was confounded with farm. This means that we have identified two risk factors which farms should focus on to reduce the risk of disease. Firstly, herds without BDD should ensure that if they cannot rear their heifers separately, they should only be reared with cattle from farms that are also free of BDD (although this is likely to be difficult to ensure). Secondly

farms with BDD should ensure that knives are disinfected effectively between cattle (though as yet there is no proven and feasible disinfection regime).

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Appendix 1: Supplementary material 1

Appendix 1: Supplementary material 2

Appendix 1: Supplementary material 3

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Table 2-1 Overview of the variables tested in the descriptive statistics for association with bovine digital dermatitis of 32,742 cows from 124 dairy herds in Taranaki, New Zealand, 09/14-02/15.

Variable	Type
1. Numbers of calves acquired from external source	Continuous
2. Source of acquired calves	Categorical
3. Number of dairy cows acquired from external source	Continuous
4. Source of acquired dairy cows	Categorical
5. Number of bulls acquired from external source	Continuous
6. Source of acquired bulls	Categorical
7. Total number of cattle acquired by the farm	Continuous
8. Transportation method	Categorical
9. Whether or not shared transportation	Categorical
10. Frequency of performing hoof trimming	Categorical
11. External staff coming to perform hoof trimming	Categorical
12. Percentage of hoof trimming done by external staff	Continuous
13. Feeding system	Categorical
14. Shed type	Categorical
15. Herd Size	Continuous
16. Month of inspecting the farms	Categorical

Table 2-2 Proportions for each of the farm level predictors remaining in the multivariable models in 114 farms in Taranaki, New Zealand, 09/14-02/15.

Predictor	Category	Frequency	Percentage
Purchasing cows from outside	No	79	69.3
	Yes	35	30.7
Young stock movement between farms	No	91	79.8
	Yes	23	20.2
Parlour type	Herringbone	75	65.8
	Rotary	39	34.2
Hoof trimming by outside staff	No	33	29.0
	Yes	81	71.0
Season of inspection	Summer	52	45.6
	Spring	62	54.4

Table 2-3 Bayesian hurdle models for the risk factors associated with bovine digital dermatitis on 114 farms in Taranaki, New Zealand, 09/14-02/15.

Predictor	Category	Posterior median (95%PI) [a]
Farm level infection		
Purchasing cows	yes vs. no	0.52 (-0.36, 1.45)
Young stock movement between farms	yes vs. no	1.42 (0.33, 2.73)
Parlour type	rotary vs. herringbone	1.16 (0.27, 2.14)
Hoof trimming by outside staff	yes vs. no	0.53 (-0.38, 1.41)
Season of inspection	spring vs. summer	0.09 (-0.76, 0.93)
Intercept		-0.65 (-1.67, 0.35)
Within infected farms		
Purchasing cows	yes vs. no	0.21 (-0.57, 0.99)
Young stock movement between farms	yes vs. no	0.21 (-0.63, 1.11)
Parlour type	rotary vs. herringbone	0.37 (-0.36, 1.13)
Hoof trimming by outside staff	yes vs. no	1.14 (0.23, 1.99)
Season of inspection	spring vs. summer	0.77 (0.05, 1.49)
Intercept		-6.14 (-7.59, -5.08)

[a] 95%PI, 95% posterior probability interval.

Table 2-4 Results of sensitivity analyses showing the effect of varying the precision of priors for negative binomial hurdle regression coefficients by +/- 50% on the posterior medians of regression coefficients and the percentage deviation from the default posterior medians of regression coefficients.

Variable	Priors variation	Posterior median (95%PI) [a]	Deviation [b]
Farm level infection			
Purchasing cows	0	0.52 (-0.36, 1.45)	0
	-50%	0.52 (-0.4, 1.48)	+0.2%
	+50%	0.51 (-0.37, 1.46)	-2.4%
Young stock movement between farms	0	1.42 (0.33, 2.73)	0
	-50%	1.46 (0.31, 2.8)	+2.3%
	+50%	1.4 (0.29, 2.67)	-1.8%
Shed type	0	1.16 (0.27, 2.14)	0
	-50%	1.17 (0.26, 2.16)	+1%
	+50%	1.14 (0.24, 2.1)	-1.9%
Hoof trimming by outside staff	0	0.53 (-0.38, 1.41)	0
	-50%	0.53 (-0.4, 1.43)	+0.2%
	+50%	0.51 (-0.38, 1.41)	-3.8%
Season of inspection	0	0.09 (-0.76, 0.93)	0
	-50%	0.09 (-0.76, 0.93)	+0.5%
	+50%	0.08 (-0.75, 0.91)	-14.2%
Intercept	0	-0.65 (-1.67, 0.35)	0
	-50%	-0.65(-1.69, 0.34)	+0.3%
	+50%	-0.61 (-1.59, 0.37)	-5.2%
Within infected farms			
Purchasing cows	0	0.21 (-0.57, 0.99)	0
	-50%	0.22 (-0.58, 1.04)	+4.7%
	+50%	0.19 (-0.56, 0.98)	-9%
Young stock movement between farms	0	0.21 (-0.63, 1.11)	0
	-50%	0.25 (-0.6, 1.18)	+19.2%
	+50%	0.19 (-0.63, 1.06)	-8.4%
Shed type	0	0.37 (-0.36, 1.13)	0
	-50%	0.42 (-0.34, 1.19)	+12%
	+50%	0.35 (-0.37, 1.07)	-5.8%
Hoof trimming by outside staff	0	1.14 (0.23, 1.99)	0
	-50%	1.2 (0.27, 2.08)	+5.3%
	+50%	1.1 (0.18, 1.92)	-3.4%
Season of inspection	0	0.77 (0.05, 1.49)	0
	-50%	0.8 (0.07, 1.56)	+4.3%
	+50%	0.76 (0.06, 1.46)	-1.6%
Intercept	0	-6.14 (-7.59, -5.08)	0
	-50%	-6.26 (-8.2, -5.21)	+2.1%
	+50%	-6.04 (-7.31, -5.04)	-1.6%

[a] 95%PI, 95% posterior probability interval.
[b] Deviation, deviation from default posterior medians.

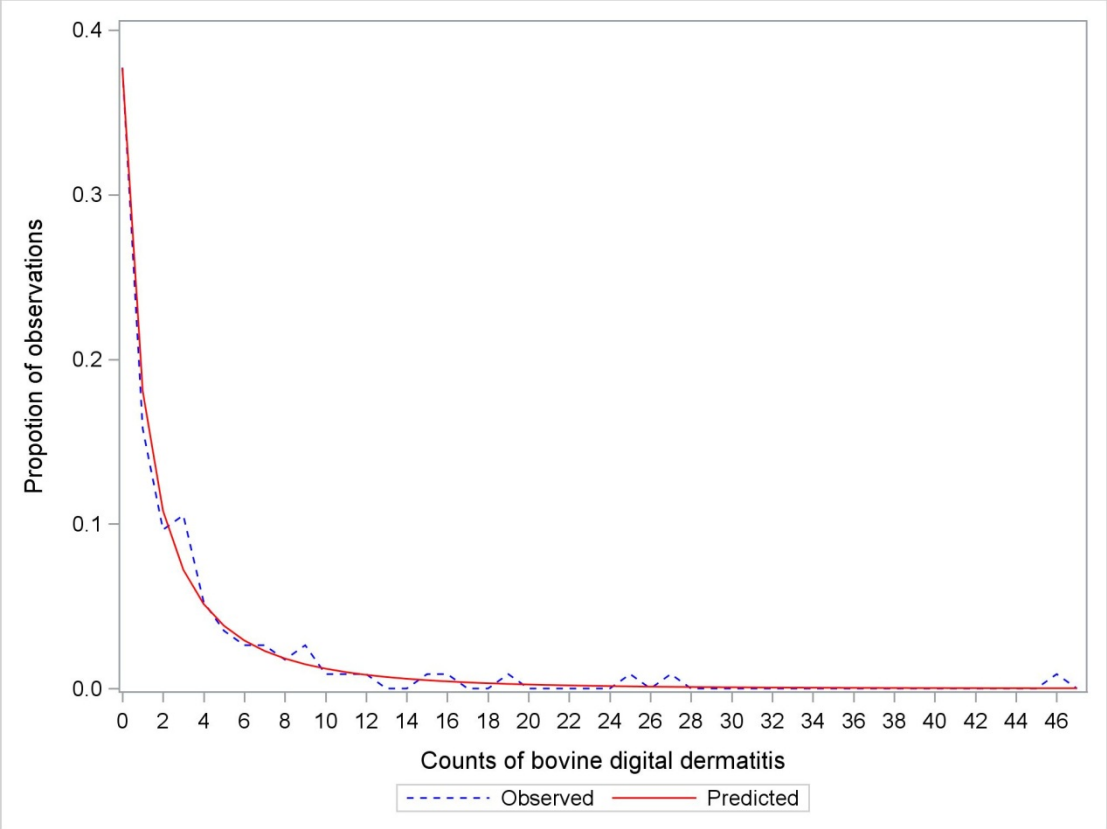

Figure 2-1 Comparison of observed and negative binomial hurdle model predicted counts of bovine digital dermatitis on 114 farms in Taranaki, New Zealand, 09/14-02/15.

Chapter 3. Effects of climates and farm management practices on bovine digital dermatitis in spring-calving pasture-based dairy farms in Taranaki, New Zealand

This chapter is prepared in the style format of The Veterinary Journal. The published manuscript is presented in appendix.

3.1. Abstract

To investigate the effect of climate and farm management practices on prevalence of bovine digital dermatitis (BDD) in spring-calving farms in Taranaki, New Zealand, whole herd assessments of BDD were made on 57 farms which had been previously identified as having cows with BDD. Assessments of BDD lesions were made on five occasions between early lactation (September 2015) and drying-off (May 2016) (at ~6-week intervals). Along with the clinical assessment, data on farm management practices were collected using questionnaires. In addition, climate data including rainfall and soil/air temperature were obtained from a local weather station. The raw temporal pattern was analysed using a generalised estimating equation method, followed by a mixed effects negative binomial model which modelled the associations between prevalence and the covariates including management practices, rainfall and soil temperature.

The highest farm and cow level prevalences were seen on the second visit (27/Oct/2015-11/Dec/2015) and were lowest on the fourth visit (29/Jan/2016-10/Mar/2016). Farms with a higher prevalence at the first visit tended to have a higher prevalence at later visits, even though the affected individuals were often different. There was thus a strong correlation (0.94) between prevalence (proportion of cows affected at each time point) and incidence (proportion of cows with new affections at each time point). Two climate measurements were found to have an association with BDD prevalence. Firstly, increased rainfall in the previous month was associated with decreased cow level prevalence; secondly, there was a quadratic relationship between prevalence and soil temperature, with prevalence increasing as soil temperature increased from 11.8°C to ~18°C and then decreasing as soil temperature increased from ~18°C to 23.9°C. In addition to the effect of climate, using outside staff to

perform hoof trimming was found to increase the risk of BDD infection (risk ratio [RR]: 2.06, 95% confidence interval [CI]: 1.05-4.06).

3.2. Keywords

Digital Dermatitis; Cattle lameness; Climate effect; Hoof trimming; Seasonality

3.3. Introduction

Bovine digital dermatitis (BDD) is a common infectious cause of lameness in housed cattle (Blowey and Sharp, 1988; Laven and Lawrence, 2006; Solano et al., 2016). In contrast, although BDD is found in herds which keep their cows at pasture for considerable periods it is much less common (Holzhauer et al., 2012). In New Zealand (NZ), where cattle are normally not housed, anecdotal evidence suggested that BDD was a rare disease with very few farms and cows affected. However a recent cross-sectional survey (Yang et al., 2017) found that the apparent herd level prevalence was 64% on 224 farms in the Taranaki region of the North Island of NZ, although the apparent cow level prevalence on these affected farms was only 1.7% (95% confidence interval [CI]: 1.4-2.1%). This large cross-sectional study lasted for 6 months (from September 2014 to February 2015). An analysis of the data suggested that more infected cows could be found on affected farms in spring than summer (Prevalence ratio [PR]: 2.16, 95% probability interval [PI]: 1.05-4.43) (Yang et al., 2018). This finding indicated that there might be a seasonal effect on BDD prevalence. However, as this was a cross-sectional study this effect was confounded by farm, with different farms being evaluated in summer and spring.

Previous research has suggested that there may be a seasonal aspect to BDD prevalence. For example, Laven and Lawrence (2006), using reports from veterinarians across the UK, reported that the summer months (June to October) all had fewer reports of BDD per month than February. This finding was consistent with previous reports of treatment for BDD from the UK (Murray et al., 1996) and reports of BDD prevalence from the Netherlands (Somers et al., 2005). However, it is likely that this seasonal effect is confounded with summer grazing as access to pasture has been shown to be associated with reduced risk for BDD (Holzhauer et al., 2006). In

fact, Holzhauer et al. (2012) in a longitudinal study of the effect of grazing on hoof disorders, including BDD, reported that the prevalence of BDD increased in the summer, and that only when the effect of grazing was included did BDD prevalence decrease in the summer compared to winter.

None of these studies evaluated the impact of season on BDD in cows that were permanently kept at pasture, nor did they link climate data to BDD prevalence. The aim of this study was to describe the temporal pattern of BDD on affected farms in Taranaki, NZ and to evaluate whether this pattern was associated with any climate data. In addition data were collected on farm management practices to identify whether they influenced the cow level prevalence of BDD and the association between climate and BDD.

3.4. Materials and Methods

3.4.1. Data collection

The study was undertaken between September 2015 and May 2016 on 57 farms in the northern part of Taranaki. All 57 farms were sampled randomly from the previously affected farms reported by Yang et al. (2017). During the study period, farms were visited approximately every six weeks, so that each farm was visited five times. The time periods for each of the five visits are summarised in Table 1. The order in which farms were screened was not random, but was based on ease of recording for the technician and the convenience of farm staff. Although the farms were repeatedly screened, the cows within each farm were not necessarily the same at each visit because of culling or the sale/purchase of cows.

All farms were screened by the same trained technician using visual assessment during milking of the hind feet only (Thomsen et al., 2008). All cows that

were being milked at the time of inspection were examined. The screening process involved careful washing of the hind feet using a hose followed by observation of the hind feet for lesions aided by the use of a head torch. Farms were screened during either the morning or the afternoon milking, two farms per day. Lesion recording was as described by Yang et al. (2017). A cow was recorded as having BDD if the technician observed at least one lesion that she thought was BDD on either hind foot. Cow level data (identification number [ID], and affected foot/feet) were recorded for cows with BDD only. The number of cows examined at each inspection was based on the farmer's records of the number of cows that had been milked during the inspection.

Along with the disease data, farmers were asked to fill in a questionnaire on farm management in the previous year (see Appendix 2: Supplementary material 1). This was undertaken only once per farm. In addition, local rainfall, and soil and air temperature data were obtained for every day from 01/June/2014 to 17/May/2016 from Ballance Agri-nutrients (**www.ballance.co.nz**). The weather station was at Tikorangi, Taranaki. The locations of the dairy herds and the weather station are shown in Figure 1. The straight line distance between the dairy herds in the study and the weather station varied from 0.5 km to 26.4 km (median 8.9 km).

In this part of Taranaki (farms around Inglewood), rainfall is significant throughout the year even in the driest month (February). The usual seasonal pattern in this region is that rainfall usually increases slightly from September (when the data collection started) to October and then decreases slowly until February, after which the rainfall keeps increasing to May (when the data collection ended). The air temperature usually increases from September to February and then decreases continually until May (https://en.climate-data.org/oceania/new-zealand/taranaki/inglewood-31450/).

3.4.2. Statistical methods

3.4.2.1. Data validation

Two datasets: “farm sheet”, “cow sheet” were created by transferring the paper records created on farm into Microsoft Excel. The “farm sheet” recorded the farm level information such as numbers of positive cases on each farm at each visit, date of visit, numbers of cows examined and data from the questionnaire on farm management practices. The “cow sheet” recorded details such as the ID of positive cows, the foot or feet involved and associated farm ID and visit ID. An additional “climate sheet” recorded the rainfall, soil and air temperature data from Ballance Agri-nutrients. The numbers of positive cows within each farm at each visit were compared between the “farm sheet” and the “cow sheet”. Hard copies of farm screening records were examined if the positive counts in both datasets were inconsistent. The accumulated rainfall in the 31 days prior to the inspection was then calculated (monthly accumulated rainfall), as was the average air/soil temperatures in the previous 7 days (average weekly air/soil temperatures).

3.4.2.2. Prevalence

The summary of prevalences included the following parameters. Firstly, overall cow level prevalence p_j at j^{th} visit was calculated as $p_j = \frac{\sum_{i=1}^{57} y_{ij}}{\sum_{i=1}^{57} n_{ij}}$, where y_{ij} was the numbers of cows with BDD lesions on i^{th} farm at j^{th} visit and n_{ij} was the numbers of cows examined on i^{th} farm at j^{th} visit. The 95% CI was calculated using a generalised estimating equation (GEE) method (Zeger et al., 1988). Secondly, the within farm prevalence was calculated as $\pi_{ij} = \frac{y_{ij}}{n_{ij}}$ for each individual farm at each visit; and then a correlation matrix was created to examine the correlation of within farm prevalence across visits. Finally, farm level prevalence was expressed as $q_j = \frac{z_j}{57}$,

where z_j was the numbers of farms with at least one cow with BDD lesion at j^{th} visit. It was then followed by a χ^2 test to see whether or not the farm level prevalence was significantly different across visits. In addition, the total number of cases (cow-times) during the whole study period was counted; and then the frequencies per cow-time that a lesion was on the right foot only, left foot only or both feet were calculated. At the individual cow level, the number of times that an individual unique cow was recorded as positive was summarised.

3.4.2.3. Incidence

The incidence was defined as the numbers of new cases divided by population at risk. A new case was defined as BDD in a cow which had not been positive before in any of the previous visits or a case which had been positive before but had been negative at the previous examination. The population at risk was defined as the number of examined animals which had been negative on the previous visit. A cow could thus be counted multiple times towards the incidence. Incidence was only calculated from the second visit on.

Similar to overall cow level prevalence, the 95%CI for overall cow level incidence were calculated using a GEE model (Zeger et al., 1988). Within farm incidence was then calculated for each visit and a correlation matrix was created to examine the correlation of within farm incidence across visits. The correlation between prevalence and incidence for individual visits and pooled visits was then calculated. The 95%CI for the correlation coefficient (pooled visits) was calculated using Fisher's z transformation.

3.4.2.4. Descriptive statistics for climate data

The central tendencies of rainfall and air/soil temperature were summarised using the mean and the median. The spread of any variable was described using the

maximum and minimum. These descriptive statistics were intended to summary by each visit.

3.4.2.5. Modelling associated factors

The raw seasonal pattern was summarised using the overall cow level prevalence at each visit. This prevalence was then modelled as a cubic polynomial function of the calendar time using "day" as unit. Let the counts Y_{ij} of diseased cows on i^{th} farm at j^{th} visit follow a negative binomial distribution:

$$Y_{ij} \sim Negbin\ (p_{ij}, r)$$

The mean count μ_{ij} can be written as:

$$\mu_{ij} = \frac{r(1-p_{ij})}{p_{ij}}$$

We then modelled the mean count μ_{ij} as:

$$\log(\mu_{ij}) = \log(N_{ij}) + k_1 {t_{ij}}^3 + k_2 {t_{ij}}^2 + k_3 t_{ij} + U_i + C$$

$$U_i \sim \text{Normal}\ (0, \sigma^2)$$

where N_{ij} is number of cows inspected on the day, U_i is the farm level random effect, C is the intercept and k_{1-3} are the regression coefficients for the time effect. So $e^{\log(\mu_{ij})-\log(N_{ij})}$ is the predicted prevalence of i^{th} farm at j^{th} visit. The model was defined as the time-only model.

A second model was then used to evaluate both the temporal effect and farm management practices. The model used was:

$$\log(\mu_{ij}) = \log(N_{ij}) + k_1 {t_{ij}}^3 + k_2 {t_{ij}}^2 + k_3 t_{ij} + \beta X_i + U_i + C$$

$$U_i \sim \text{Normal}\ (0, \sigma^2)$$

where β is the regression coefficient vector not including the intercept and X is the farm management practices vector. A forward selection process was used to select management practice predictors in the multivariable model. The predictor with the

largest Wald statistic was fitted into the time-only model first and the process repeated with the other predictors in order of Wald statistic until none met the entry criteria; i.e. predictor had a P value ≤ 0.05 and the Bayesian information criterion (BIC) of the model did not increase when the predictor was added (Schwarz, 1978).

For the climate analysis, the predicted prevalence from the time-only model was plotted against both the monthly accumulated rainfall and weekly air/soil temperatures. Guided by the plots, a negative linear relationship between monthly rainfall and BDD prevalence, and a quadratic relationship between weekly air/soil temperatures and BDD prevalence were expected. Air and soil temperature were highly correlated, so soil temperature was used to avoid collinearity as it was anticipated that soil temperature might have a more direct effect on cows' feet than air temperature. The climate model was defined as:

$$\log(\mu_{ij}) = \log(N_{ij}) + \gamma * rainfall_{ij} + \theta_1 * soil\_T_{ij} + \theta_2 * soil\_T_{ij}^2 + \beta X_{ij} + U_i + C$$

$$U_i \sim \text{Normal}\,(0, \sigma^2)$$

where γ and θ_{1-2} are the regression coefficients for rainfall and soil temperature. The climate model was validated by plotting the model predicted temporal pattern against the raw temporal pattern summarised in the prevalence section. The analyses were performed using Stata/IC 13.1 (StataCorp, USA).

3.5. Results

3.5.1. Prevalence

The number of farms on which BDD was observed were 33 (57.9%), 48 (84.2%), 43 (75.4%), 25 (43.9%) and 26 (45.6%), for visits 1 to 5, respectively. Across visits, the farm level prevalences were significantly different (p <0.001). Over

the whole inspection period, cows were not identified as having BDD on 2/57 farms. At the observation level, 938 cow-times were recorded as positive. Of these 938 cow-times, 259 (27.6%) lesions were recorded on left rear feet only; 345 (36.8%) on right rear feet only and 334 (35.6%) on both rear feet.

At the cow level, 646 unique cows were identified as BDD positive. Of these positive cows, 469 cows were recorded as positive only once, 99 cows were recorded twice, 51 cows three times, 17 cows four times and 10 cows five times. At each visit, the total cows examined on the 57 farms were 17 941, 18 789, 18 739, 17 766 and 16 400, respectively. The overall cow level prevalence is shown in Figure 2, and within farm prevalence in Figure 3. Within farm prevalence was highly correlated across visits (Table 2).

3.5.2. Incidence

During the inspection period, 553 cow-times were identified as new positives. Using the first visit as the base, there were 249, 154, 48, and 102 new cases at the second, third, fourth and fifth visits respectively. The overall cow level incidence is illustrated in Figure 2. At the overall cow level, the incidence demonstrated a similar pattern to prevalence. Comparing the pattern of incidence to prevalence for individual farms (Figure 3) also indicated that incidence was correlated with prevalence. The Pearson correlation coefficients between incidence and prevalence at visits 2-5 were 0.92, 0.96, 0.91 and 0.98, respectively and for pooled visits 0.94 (95%CI: 0.93 - 0.96). An auto-correlation of within farm incidence was also detected (Table 3).

3.5.3. Farm management and climate

The only management practice which had a significant effect on BDD prevalence was the use of external staff to do hoof trimming (RR: 2.06, 95%CI: 1.05-4.06). The summary statistics of the rainfall and soil temperature at each farm visit are displayed in Table 4. The relationship between the BDD prevalence and climate factors, accounting for the effect of hoof trimming practice is presented in Figure 4. There was an obvious negative relationship between monthly accumulated rainfall and BDD prevalence, i.e. the risk of BDD decreased by 0.82 (95%CI: 0.71-0.97) for every one standard deviation (37.2mm) increase in the monthly accumulated rainfall. BDD prevalence increased when average weekly soil temperature increased from 11.8°C to approximately 18°C and the prevalence decreased when average weekly soil temperature increased from approximately 18°C to 23.9°C. Model validation showed that predicted seasonality had the same pattern as the raw seasonality, although the model underestimated the overall cow level prevalence during the third visit (Figure 5).

3.6. Discussion

This is the first longitudinal study of BDD in NZ, which is consistent with evidence that BDD is a dynamic disease in dairy cattle that some lesions could resolve without treatment after persisting for long period (Krull et al., 2016b). It showed that cow level prevalence/incidence as well as farm level prevalence of BDD could change over time during a single lactation. Nevertheless, a farm with a relatively high prevalence at the beginning of lactation tended to have a relatively high infection level later in lactation, even though most of the infected cows were different at each visit. This was because prevalence and incidence were highly correlated, so although

on farms with a high prevalence of disease, more cows became apparently lesion-free between inspections this was balanced by more cows developing observable lesions.

The raw seasonal pattern suggested both farm and cow level prevalences peaked in spring (2nd visit) and then decreased in summer (3rd-5th visits). This finding is consistent with the findings of Yang et al (2018), and also those of Holzhauer et al. (2012) who reported that in the Netherlands compared to the baseline prevalence in February (late winter) the odds of a cow at pasture being observed with BDD was lower in May and even lower in August (summer) .

The impact of lactation stage was not included in this study, although it has been shown to be associated with BDD prevalence with Argáez-Rodríguez et al. (1997) reporting that the highest prevalence of BDD was seen in the first month after calving; while Holzhauer et al. (2006) suggested peak lactation was the period with the highest risk. However, in NZ, the seasonal nature of dairy farming means that lactation stage and calendar date are highly collinear at the farm level, so the apparent effect of time could actually be an effect of lactation stage. However the analysis of the effect of climate on BDD prevalence suggests that in NZ the apparent effect of time is actually mediated by climate effects, consistent with the links between climate and seasonality of BDD suggested by Holzhauer et al. (2006). The predicted prevalence from the time-only model showed a clear relationship with rainfall and a suggestive relationship with soil temperature. When these climate variables replaced calendar date in the model, they were found to have significant associations with BDD prevalence, and this model closely predicted the observed seasonal pattern. Thus in pasture-based cows changes in BDD infection at the individual and farm level may be mediated, at least in part, by changes in rainfall and soil temperature.

Further research is required to establish how these climate factors alter the prevalence of BDD, as this analysis only identifies a potential connection and provides limited evidence as to pathogenesis. Both the rainfall and temperature effect seen in this study are in contrast to what would be expected based on housed cattle, as BDD is more common in the winter (DeFrain et al., 2013) when it is colder and, often, wetter. In contrast this study found that ~18°C was the optimal temperature for BDD development and that wetter conditions were associated with decreased BDD prevalence. DeFrain et al. (2013) suggested that the link between BDD and temperature was down to increased exposure to harsh environments and less efficacious footbathing. In this study none of the farms were actively controlling BDD, so our findings may be more representative of the natural biology of the pathogens causing BDD.

The impact of rainfall was unexpected as prolonged exposure to moisture is necessary for the establishment and transmission of BDD (Krull et al., 2016a). In addition, interdigital necrobacillosis, the other main infectious cause of lameness in cattle, is often linked to wet underfoot conditions, especially in cattle at pasture because such conditions macerate the skin allowing the causative bacteria to reach the deeper tissues in the interdigital space (Van Metre, 2017), a process which is similar to that used in the artificial induction model of BDD used by Krull et al. (2016a). However, Laven and Lawrence (2006) reported that the seasonality of BDD and interdigital necrobacillosis were not the same, especially during the summer grazing period, so interdigital necrobacillosis may not be as good model for BDD as would appear. One potential route by which increased rainfall could increase is by improving hygiene, which is strongly associated with BDD prevalence (Relun et al., 2013; Somers et al., 2005), as heavier rainfall may wash dirt on the feet away. This

suggestion needs further investigation but it is consistent with the finding of Yang et al. (2019) that BDD was absent on the West Coast of NZ – a region with heavy rainfall on the South Island where cows' feet were observed to be much cleaner than those in other regions. This is also consistent with anecdotal data from pasture-based herds in Chile, where footbath control of BDD is effective during periods of wet weather but much less effective during a drought (personal communication R.N. Chesterton).

In addition to the climate effects, we also showed that farms which used outside staff, principally veterinarians, to treat lame cows had significantly higher prevalence of BDD over the study period. This finding has been reported by Wells et al. (1999) and Yang et al. (2018). The model did not identify any other management practices which were associated with increased BDD prevalence in this study, although a previous study in the same region reported rearing heifers together with heifers from other properties was a risk factor of this disease (Yang et al., 2018). Main reason for the difference is that rearing heifers with heifers from other properties only increased the risk of introduction of BDD, but not the cow level prevalence within herds. In this study, all farms are BDD positive, hence, not detecting such an effect agrees with Yang et al. (2018).

Other predictors associated with cattle movement were also not identified as risk factors in this study. Out of 57 farms, 31 had purchased replacement heifers in the previous year, but with little variation in numbers bought as proportion of a herd. Among those farms, 48/57 farms had leased bulls for breeding in the previous year – again with limited variation (see Appendix 2: Supplementary material 2). Either continuous or categorical forms of the cattle purchasing/leasing predictors were not significant in the multivariable analysis, therefore excluded in the final model.

This study may provide a guide for managing BDD on seasonally calving pasture-based farms. Firstly, the best time to screen BDD is probably mid-spring to early summer (late October to end of January in NZ), as the prevalence of BDD is likely to be at its peak during this period. Control should focus on: 1) Strict disinfection, between cows, of all knives and equipment used for hoof trimming (especially if outside staff are used); 2) in dry weather hosing cows' feet to remove attached mud/slurry may be protective as it mimics the heavy rainfall environment; and 3) when soil temperature is around 18°C, the use of a regularly cleaned and well drained stand-off pad may be useful to minimise disease spread, especially when it is dry.

3.7. Conclusions

The study described the seasonal pattern of BDD prevalence and showed that rainfall and soil temperature are both associated with BDD prevalence. In pasture-based herds screening for BDD in mid-spring to early summer may be the optimal time as BDD prevalence is likely to be at its peak.

3.8. Conflict of interest statement

None of the authors has any financial or personal relationships that could inappropriately influence or bias the content of the paper.

3.9. Acknowledgements

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Appendix 2: Supplementary material 1

Appendix 2: Supplementary material 2

3.10. References

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Table 3-1 Five farm visits with their corresponding periods in Taranaki, New Zeleand, 2015-2016.

Visit	Period
1	07/Sep/2015-29/Oct/2015
2	27/Oct/2015-11/Dec/2015
3	08/Dec/2015-29/Jan/2016
4	29/Jan/2016-10/Mar/2016
5	10/Mar/2016-04/May/2016

Table 3-2 Correlation matrix to demonstrate the correlation of the within farm prevalence of bovine digital dermatitis across the visits in Taranaki, New Zealand, 2015-2016.

Visit	1	2	3	4	5
1	1.00	0.61	0.70	0.74	0.76
2	0.61	1.00	0.77	0.58	0.52
3	0.70	0.77	1.00	0.67	0.61
4	0.74	0.58	0.67	1.00	0.71
5	0.76	0.52	0.61	0.71	1.00

Table 3-3 Correlation matrix to demonstrate the correlation of the within farm incidence of bovine digital dermatitis across the visits in Taranaki, New Zealand, 2015-2016.

Visit	2	3	4	5
2	1.00	0.61	0.70	0.74
3	0.61	1.00	0.77	0.58
4	0.70	0.77	1.00	0.67
5	0.74	0.58	0.67	1.00

Table 3-4 Summary statistics of rainfall and soil temperature data at each farm visit from 07/Sep/2015 to 04/May/2016 in Taranaki, New Zealand.

Variable (unit)	Mean	Median	Minimum	Maximum
Visit 1 (07/Sep/2015-29/Oct/2015)				
Rainfall (mm)	85.8	60.6	15.2	156
Soil temperature (°C)	13.8	14	11.8	16.7
Visit 2 (27/Oct/2015-11/Dec/2015)				
Rainfall (mm)	33.6	29.2	14.2	74.6
Soil temperature (°C)	17.8	17.5	16.2	21.5
Visit 3 (08/Dec/2015-29/Jan/2016)				
Rainfall (mm)	61.3	63.6	39.2	123.4
Soil temperature (°C)	21.4	21.6	19.2	23.9
Visit 4 (29/Jan/2016-10/Mar/2016)				
Rainfall (mm)	95.3	97	62.8	130.4
Soil temperature (°C)	22.5	22.7	19.2	23.9
Visit 5 (10/Mar/2016-04/May/2016)				
Rainfall (mm)	82.5	90.2	21.4	152.8
Soil temperature (°C)	19.1	19.5	16.1	21.4

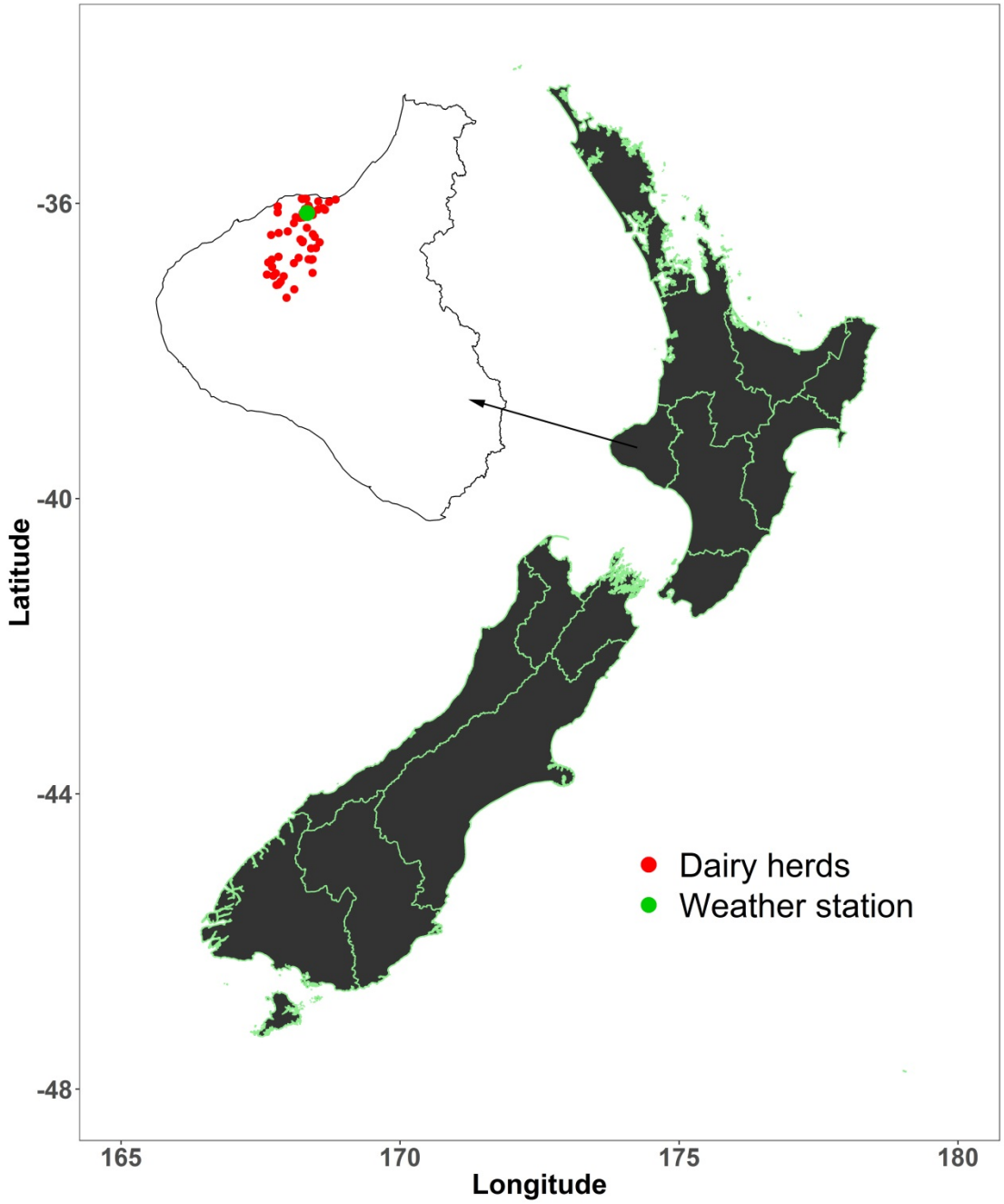

Figure 3-1 Overview of Taranaki region in New Zealand and the locations of the dairy herds enrolled in the study and weather station.

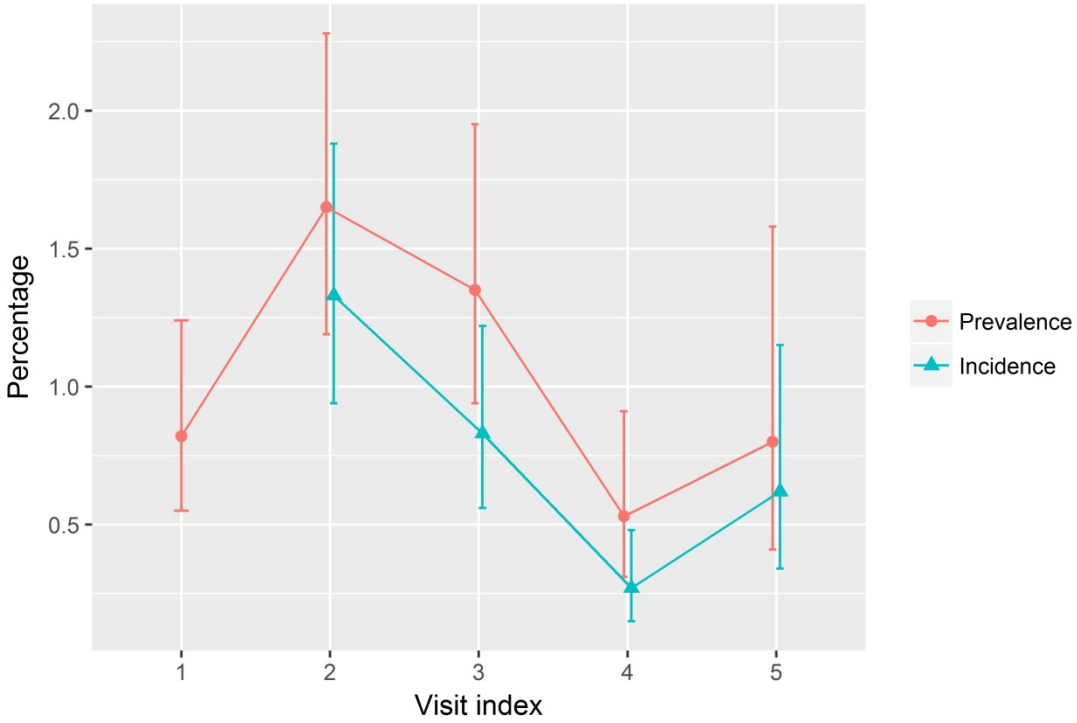

Figure 3-2 Overall cow level prevalence/incidence of bovine digital dermatitis on 57 farms at each visit in Taranaki, New Zealand, 2015-2016.

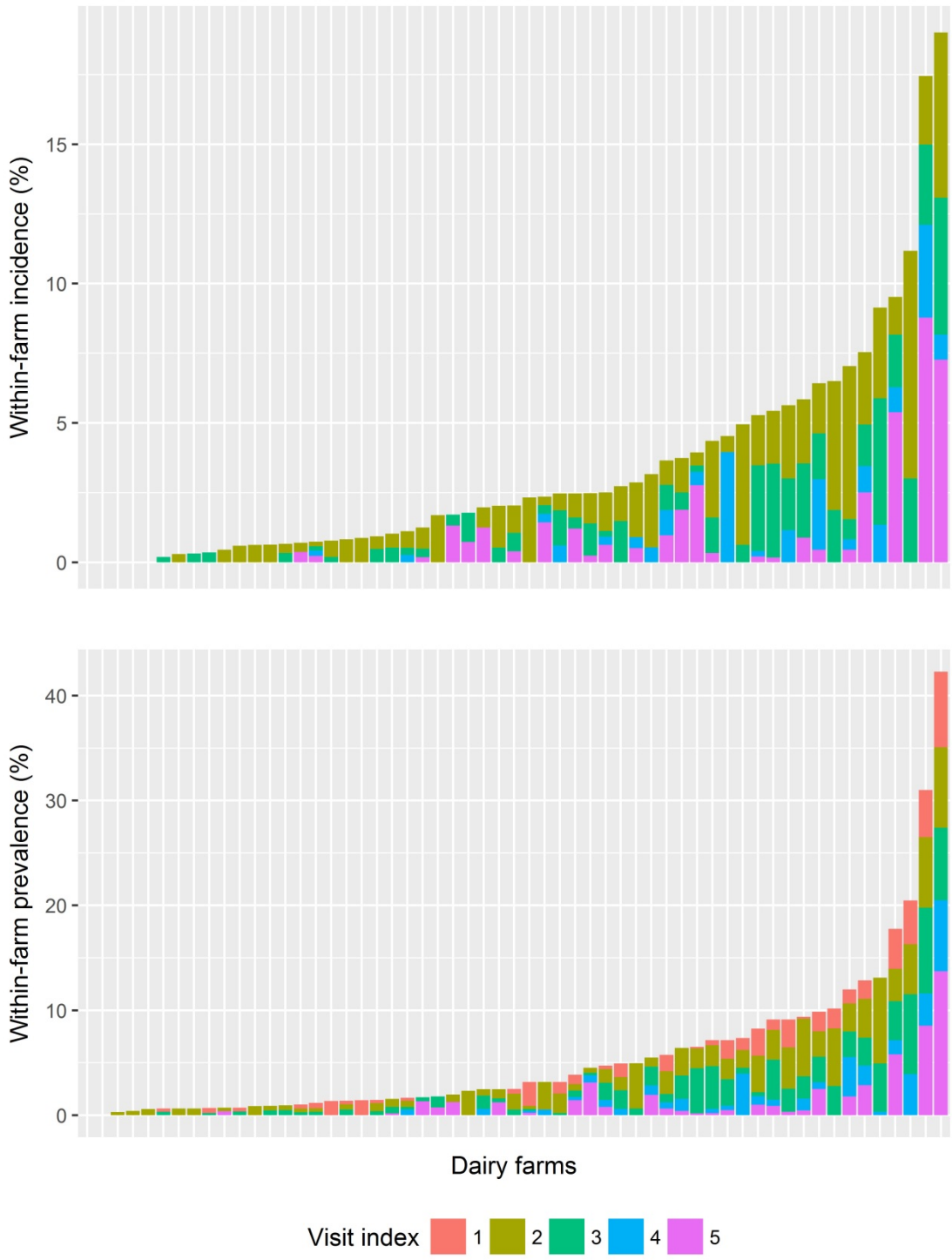

Figure 3-3 Within farm prevalence/incidence of bovine digital dermatitis on 57 farms at each visit in Taranaki, New Zealand, 2015-2016.

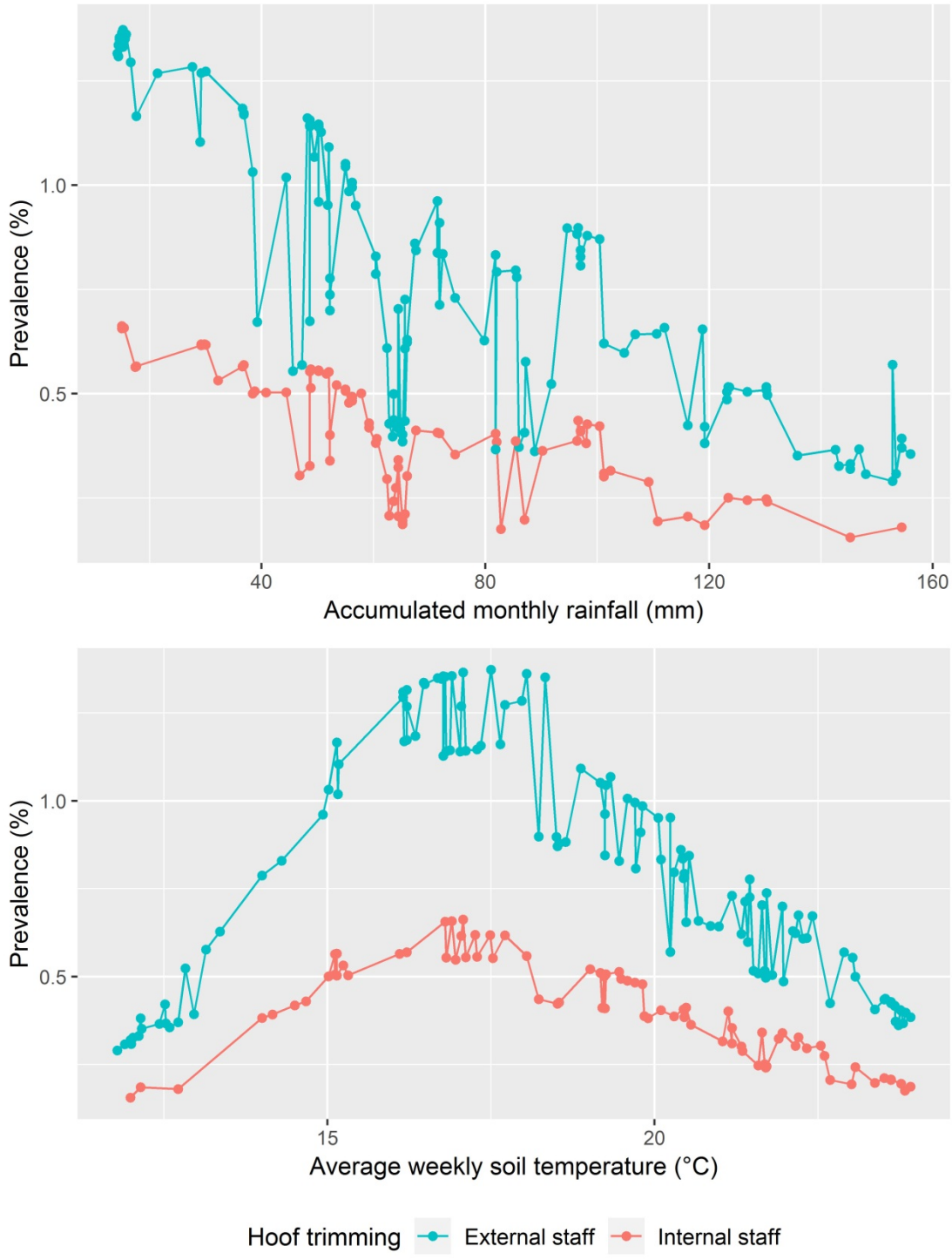

Figure 3-4 Associations between the predicted cow level prevalence of bovine digital dermatitis and climate factors including the monthly accumulated rainfall and average weekly soil temperatures before the day of farm screening. The predicted pattern was stratified by two groups: hoof trimming by external and internal staff.

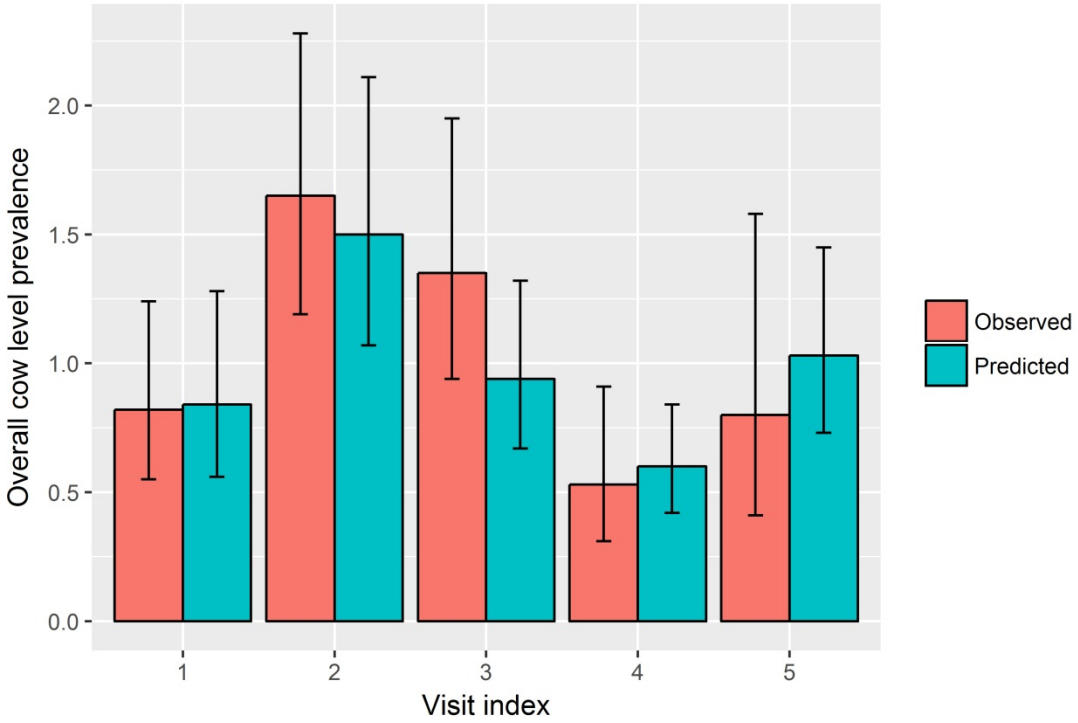

Figure 3-5 Comparison between the model predicted seasonal pattern and raw seasonal pattern using prevalence as a measurement of bovine digital dermatitis frequency.

Chapter 4. Estimating the herd and cow level prevalence of bovine digital dermatitis on New Zealand dairy farms: A Bayesian superpopulation approach

This chapter is prepared in the style format of Preventive Veterinary Medicine. The published manuscript is presented in appendix.

4.1. Abstract

A cross-sectional study of 127 dairy herds distributed across four regions of New Zealand (NZ) was conducted to estimate the regional herd-level prevalence of bovine digital dermatitis (BDD) and the prevalence of cows with visible lesions within affected herds. Each herd was visited once during the 2016-2017 lactating season and the rear feet of all cows in the milking herd were examined to detect the presence of visible BDD lesions. Of the 127 herds examined, 63 had at least one cow with a detected BDD lesion. Of the 59 849 cows observed, 646 cows were observed with BDD lesions. All of the herds in which BBD was detected were located in three of the four regions (Waikato, Manawatu and South Canterbury). No convincing lesions were observed on the West Coast. The probability of BDD freedom on the West Coast was predicted to be 99.97% using a Bayesian latent class model. For the three regions where BDD lesions were observed, the true herd level and cow level prevalences were estimated using a Bayesian superpopulation approach which accounted for the imperfect diagnostic method. Based on priors obtained from previous research in another region of NZ (Taranaki), the true herd level prevalences in Waikato, Manawatu and South Canterbury were estimated to be 59.2% (95% probability interval [PI]: 44.3%-73.9%), 43.3% (95%PI: 29%-59%) and 65.9% (95%PI: 49.5-79.9), respectively, while the true median within-herd prevalences were estimated as 3.2% (95%PI: 2%-5%), 1.7% (95%PI: 0.9%-3.1%) and 3.7% (95%PI: 2.4%-5.5%), respectively. All of these estimates except for the true herd level prevalence in Manawatu were fairly robust to changes in the priors. For the Manawatu region, changing from the prior obtained in Taranaki (the best estimate of the herd level prevalence = 60%, 95% sure > 40%) to one where the mode was 50% (95% sure < 80%) reduced the posterior from 43.3% to 35.2% (95%PI: 20.1%-53.5%). The

marked variation in BDD prevalence between regions and between farms highlights the need for further exploration into risk factors for disease.

4.2. Keywords

Bovine digital dermatitis; Dairy cattle, Prevalence, Disease freedom, Imperfect diagnostic method, New Zealand

4.3. Introduction

Bovine digital dermatitis (BDD) is an infectious disease of the feet of cattle (Evans et al., 2009; Krull et al., 2016), and the most commonly observed foot disease on many dairy farms (Solano et al., 2016). The impact of BDD lesions can vary from causing mild discomfort to significant pain (O Callaghan et al., 2003; Archer et al., 2010). In addition, BDD has also been associated with reduced productivity and reproductive performance (Relun et al., 2013b; Gomez et al., 2015).

BDD is significantly less common in pasture-based systems (Laven and Lawrence, 2006), but has been reported in many countries where cattle are permanently kept at pasture including Chile (Rodriguez-Lainz et al., 1998), Australia (Milinovich et al., 2004) and New Zealand (Vermunt and Hill, 2004). Ten years after the first observation of BDD in New Zealand (NZ) in response to an apparent increase in reports of BDD, a large scale cross-sectional study was conducted in Taranaki, a region on the west coast of the North Island of NZ to investigate prevalence using visual observation during milking (Yang et al., 2017a, b). This study showed that 1) over a period of 10 years, BDD had become a common disease at the herd level, with nearly 70% of Taranaki dairy farms having at least one cow with a BDD lesion; 2) visible lesions were rare on affected farms, with the average proportion of cattle with such lesions being < 3%, although some farms had as many as 13% of cows affected; and 3) the spatial distribution of BDD across northern Taranaki was random, with no evidence that the risk of disease was related to the presence or absence of disease on nearby farms.

Based on the high herd level of prevalence of BDD in Taranaki, it was decided to investigate the prevalence of BDD at the cow and herd level in other regions of NZ, by observing cattle for BDD lesions during milking, as had been done in Taranaki.

However, estimating the true prevalence of BDD can be challenging because the detection of BDD lesions using visual inspection during milking is an imperfect diagnostic method. Small lesions are easily missed, resulting in foot inspection having limited diagnostic sensitivity (Yang et al., 2017a). There can also be significant differences between milking parlours in the ease of detection of BDD lesions (Yang et al., 2018). Finally, especially for small lesions, the interpretation of changes in the heel bulb area is subjective, and therefore prone to observer bias (Vink et al., 2009). Thus, in order to use the data from the survey to make inferences as to the true prevalence of BDD in NZ at the cow, herd or regional level, the sensitivity and specificity of visual inspection for BDD must be factored into models.

The sensitivity and specificity of visual assessment of BDD lesions in the milking parlour (parlour assessment) could be estimated by comparing the results from assessment in the parlour to another reference test, such as the assessment of BDD in the lifted foot with the cow in a trimming crush. However, comparing these two methods on multiple farms as part of a large-scale survey is not feasible, precluding the use of a standard two tests Bayesian latent class analysis (Johnson et al., 2001). However, two recent papers (McAloon et al., 2016; Yang et al., 2017a) produced estimates of true prevalences at both herd and animal level from data where a single test had been used alone on multiple populations using a Bayesian latent class model. The prevalence estimates in these papers were based on the binomial approach which assumes that the sampled population is infinite. This assumption can be relaxed when the population size (N) far exceeds the sample size (n), i.e. $n/N < 0.05$ (Jordan and McEwen, 1998; Branscum et al., 2004). However, both analyses used data from testing entire herds, thus both analyses ignored the finite nature of dairy herds. To overcome this problem, Jones and Johnson (2016), presented a Bayesian

superpopulation approach that justifies the use of a modified binomial method to make inferences on finite populations. This approach assumes a number of superpopulations have been sampled independently from the population of the superpopulations and thus each finite dairy herd can be regarded as a random sample drawn from its own superpopulation. This then allows prevalence estimates to be made using data from entire herds without using a statistical method whose assumptions are violated. A brief explanation of how this model is implemented is in the statistical analysis section below.

The aim of this study was thus to collect data on the prevalence of BDD in four regions of NZ using visual observation during milking and to then use the Bayesian superpopulation approach to provide estimates of true herd and animal level prevalences for those regions as well as to compare those results with those from the previous survey in Taranaki.

4.4. Materials and methods

4.4.1. Study recruitment

A region-by-region sampling scheme was adopted. The four regions chosen for sampling were: Waikato, Manawatu, the West Coast and South Canterbury shown in Figure 1. Waikato was chosen as it is the predominant dairy region of NZ; Manawatu was chosen for convenience as Massey University is located in the Manawatu; the West Coast was selected due to its differences from other regions in climate, geography and farm management; Canterbury was chosen as a representative region for the large South Island (SI) herds kept on predominantly irrigated pasture. To minimise travel distances only herds in South Canterbury were used for the latter region.

Within each region, the number of herds required to be examined in order to estimate herd level prevalence was calculated using a formula with a correction for finite populations (see "Finite Population Correction" in Naing et al., 2006). We assumed that the herd level prevalence of BDD in each region would be approximately 60% (Yang et al., 2017b), and that we would like to be 95% certain that our estimate was within ± 15% of the true/actual herd level prevalence (the formal definition of the precision term "15%" can be seen in the section "Assumption of Normal Approximation" in Naing et al., 2006). The precision term was decided based on the workload and minimising impact of seasonal differences on the disease (Holzhauer et al., 2012). The total numbers of herds in Waikato, Manawatu, the West Coast and South Canterbury were 3507, 555, 376 and 304, respectively (LIC, 2016). This calculation suggested that 41, 38, 37 and 36 herds should be sampled in Waikato, Manawatu, the West Coast and South Canterbury, respectively. Within each herd, all cows that were present in the milking herd on the sampling date were examined.

4.4.2. Data collection

The regions were first visited in a north/south order (based on planned start of calving to maximise the proportion of the milking herd present at inspection). Half the calculated herds were visited in each region before moving on to the next. The intention was to then reverse the order starting in South Canterbury and going north.

Visual assessment was used to identify lesions as per Yang et al. (2017b). All inspections were undertaken by the first author. Only the rear feet of cattle were inspected as very few cows have lesions on the front feet only (Laven and Proven, 2000; Solano et al., 2016). During inspection, cows' rear feet were hosed carefully, after which a hand torch was used to aid observation. Presence/absence of lesions was

recorded for each cow. If the examiner was unsure whether lesions were BDD or not, colour pictures of the suspicious lesions were taken and discussed with the other authors (Müller and Laven) and Neil Chesterton (a NZ cattle lameness expert). Illness during data collection disrupted the plan so that at the end of data collection (18/Feb/2017) data had been collected from 40, 41, 27 and 19 herds in Waikato, Manawatu, the West Coast and South Canterbury, respectively.

4.4.3. Statistical analyses

Data from each region were analysed separately. An affected herd was defined as a herd with at least one cow with a visible BDD lesion). The apparent herd level prevalence (i.e. the proportion of affected herds / number of sampled herds) and the apparent within-herd prevalence for each herd (i.e. number of cows with lesions / number of cows being milked) were calculated. Since the apparent within-herd prevalences did not appear to follow normal distribution, the median within-herd prevalence was used as point estimate of cow level prevalence.

The true prevalences of BDD at the herd level and animal level were then modelled using the Bayesian superpopulation approach. Inferences of interest were the herd level prevalence, the distribution of within-herd prevalences in affected herds, and the median among within-herd prevalences.

The modelling process was as follows: the first assumption was that each herd was sampled from a superpopulation of herds, and that each superpopulation was sampled independently from the population of superpopulations. The proportion of the superpopulations that were BDD affected was defined as τ (analogous to the herd level prevalence). Given that the i^{th} superpopulation was affected, the prevalence π_i

(analogous to the within-herd prevalence) was drawn from a prevalence distribution (analogous to the distribution of the within-herd prevalence of affected herds).

Then for the i^{th} herd, the number of cows with observable lesions of BDD was y_i and the total number of cows examined in the herd was n_i. The first part of the model was then constructed as:

$$\begin{aligned} y_i \mid p_i, z_i &\sim \text{Binomial}\ (n_i, p_i) \\ p_i &= z_i\pi_i\eta + (1 - z_i\pi_i)(1 - \theta) \\ z_i \mid \tau &\sim \text{Bernoulli}\ (\tau) \\ logit(\pi_i) \mid \mu, \sigma &\sim \text{Normal}\ (\mu, \sigma^2) \end{aligned} \qquad (1)$$

where p_i is the probability of a cow being test positive in the i^{th} superpopulation and thus the apparent prevalence of the i^{th} herd given the infection was present in the i^{th} superpopulation, i.e., $z_i = 1$; η and θ were the test sensitivity and specificity. The prevalence distribution of the affected herds was modelled using a logit-normal distribution, where the median of the prevalence distribution is $\tilde{m} = e^{\mu}/(1 + e^{\mu})$ and σ described the variability among prevalences. This part of the model is identical to binomial models for diagnostic outcome data where the n_i animals are regarded as a sample from a very large herd, rather than having sampled the entire herd of size n_i, as is the case here. Models for the former situation with prevalence distributions similar to ours can be found in Hanson et al. (2003), Dhand et al. (2010) and Verdugo et al. (2014).

The second part of the superpopulation model was constructed as follows. The true number of cows with BDD lesions (Y_i^+) when there were y_i test-positive cows was modelled as:

$$\begin{aligned} Y_i^+ \mid y_i, \pi_i, z_i, \eta, \theta &\sim \text{Binomial}\ (y_i, \kappa_i^+) \\ \kappa_i^+ &= \frac{z_i\pi_i\eta}{p_i} \end{aligned}$$

where κ_i^+ was the positive predictive value for the test in the i^{th} superpopulation. And similarly, the number of false negatives among $n_i - y_i$ test negative cows was

$$Y_i^- \mid y_i, \pi_i, z_i, \eta, \theta \sim \text{Binomial}\ (n_i - y_i, 1 - \kappa_i^-)$$

$$1 - \kappa_i^- = \frac{z_i \pi_i (1 - \eta)}{1 - p_i}$$

where $1 - \kappa_i^-$ was the false negative rate, that is κ_i^- was the negative predictive value. As all the milking cows of any herd were examined, the unsampled portion of the herd was zero, therefore, the number of truly BDD lesion-positive cows in the i^{th} herd was $Y_i = Y_i^+ + Y_i^-,$ and the modelled unknown true within-herd prevalence of finite herd i was the ratio of Y_i/n_i. The Bayesian procedure would involve obtaining an estimate and probability interval for these using Markov chain Monte Carlo approximations to posterior (predictive) inferences.

We observe in passing that if n_i was the sample size from a herd of size $N_i > n_i$, there would now be U_i unobserved and unknown BDD affected animals out of the remaining $N_i - n_i$ non-tested animals. In the superpopulation approach, U_i is modelled as a binomial $(N_i - n_i,\ \pi_i)$ random variable, which is independent of Y_i. This would then complete part 2 of the superpopulation model described in section 2.1 of Jones and Johnson (2016). The OpenBUGS code for analysing one of the regions using this model is given in the Appendix.

Priors for τ and $\tilde{m}$ were obtained from the Taranaki data (Yang et al., 2017a, b). Those priors were used in all the regions where visible lesions were present, i.e. Waikato, Manawatu and South Canterbury. To be conservative, we set smaller values for τ, i.e. beta (10.9, 7.6), than the herd level prevalence reported in Taranaki. This beta distribution reflected our best estimate for herd level prevalence was 0.6 and we were 95% sure it was > 0.4. We set beta (4.55, 115.76) for $\tilde{m}$ which means the

expected median within-herd prevalence was 0.03 and we were 95% sure < 0.07. A uniform (0, 1) prior was set for σ.

Prior information for the sensitivity (η) and specificity (θ) was obtained from a NZ study that estimated these parameters using a latent class Bayesian binomial model (Yang et al., 2017a). The Yang et al. (2017a) method is specified in the same way as the initial part of the specification for the superpopulation approach. Since this approach parameterises the sensitivity and specificity in the same way as in the latent class Bayesian binomial model, the outputs of Yang et al. (2017a) could be used to form a highly informative prior for the current analysis.

However, Yang et al. (2017a) found that their posterior for sensitivity was quite sensitive to their choice of prior, thus using their posterior as our current prior for sensitivity might be questioned. Therefore, the outputs of other studies were also considered in our prior specification (see Table 1). Most of the studies listed in Table 1 have similar sensitivity estimates to that reported in Yang et al. (2017a). On the other hand, Relun et al. (2011) reported a much higher sensitivity (90%) than was reported in these studies. However, since in this study the lesions were small and the time spent on inspecting cows' feet was limited (both of which reduce the sensitivity, Thomsen et al. (2008)), Relun et al. (2011)'s result was discounted intentionally by not allowing for that high a sensitivity in our prior. Since the other studies have consistent estimates, we preferred to base our best estimate and corresponding choice of beta prior on those studies rather than include Relun et al. (2011). Our best estimate for η was 65% and we were 95% sure it was greater than 50%, which leads to a beta (20.99, 11.77).

In regard to specificity, the result reported by Yang et al. (2017a) was prioritised. Unlike the posterior for sensitivity being sensitive to its prior, the posterior

for specificity was robust (approaching 100%, with little uncertainty) by specifying a range of priors (Yang et al., 2017a). Such a high value of specificity in pasture-based dairy cattle could also be seen in the work of Rodriguez-Lainz et al. (1998) where the same diagnostic method was used for cattle in Chile. However, the specificity reported in Chile had wider 95% interval than the 95% credible interval reported in NZ. Therefore, to utilise information from both studies, our best estimate for θ was 99% and we were 95% sure it was more than 95% which leads to a beta (88.28, 1.88) prior. The priors for both η and θ were intended to be conservative (See supplementary materials for the prior distribution plots).

Because the model with only one imperfect test is not identifiable, inferences will be sensitive to the selected priors. As the number of sampled herds per region were low, to get reliable herd level prevalence estimates, it was important to assess how sensitive the posterior for τ was to its prior specification. Two different priors were thus placed on τ. The first was beta (3.26, 3.26) which indicated the mode was 0.5 and we were 95% sure it was less than 0.8, and at the same time, 95% sure it was greater than 0.2; the other was beta (2.35, 4.14) indicating the mode was 0.3 and we were 95% sure it was greater than 0.1. It was also of interest to see the effect of prior modifications of sensitivity and specificity on posterior inferences for prevalences. Therefore the best estimate for sensitivity was increased to 90% (Relun et al., 2011) by holding 5th percentile being 50%, which leads to a beta (5.38, 1.49) prior. Both Thomsen et al. (2008) and Relun et al. (2011) reported lower specificities compared to the other studies summarised in Table 1, their results were considered to form a pessimistic prior for specificity where the best estimate was decreased to 85% with 5th percentile being 75%. This estimate led to a beta (46.35, 9) prior.

For a region (the West Coast) with no visible lesions, the model was set up to examine how certain we were that the region was free of BDD. In this instance, the herds in that region were combined as one large sample as the data contained no information about the distribution of prevalences across herds.

The observed number of BDD cows, y, followed a binomial distribution with apparent prevalence q and number of cows examined h. The apparent prevalence was then linked to sensitivity (η), specificity (θ) and the true prevalence $d * \tilde{\pi}$ which depends on the infection status of the region, d, where $d \sim \text{Bernoulli}(\tilde{\tau})$, and the within region prevalence $\tilde{\pi}$, if the region is affected. Here, $q = d\tilde{\pi}\eta + (1 - d\tilde{\pi})(1 - \theta)$. Priors for $\tilde{\pi}$, $\tilde{\tau}$, η and θ were the same as used previously, for example beta (10.9, 7.6) for $\tilde{\tau}$ and beta (4.55, 115.76) for $\tilde{\pi}$. This model was then used to simulate the number of BDD animals in the unsampled large population, using a Poisson approximation to the underlying binomial. To create a Boolean variable that counted the number of BDD animals ≥ 1, we used the step() function in OpenBUGS. The monitored mean of 1-step() is the point estimate of the probability that number of animals with BDD lesions was less than one in the unsampled population. OpenBUGS code for analysing the data from the West Coast is also given in the Appendix.

All models were fitted using OpenBUGS (Spiegelhalter et al., 2007). To assess model convergence, we ran three chains with different sets of initial parameter values and examined the corresponding Brooks-Gelman-Rubin plots (Brooks and Gelman, 1998).

4.5. Results

4.5.1. Observations

During the observation period, 59 849 cows in 127 herds were examined. Lesions consistent with BDD were observed in 646 cows in 63 herds. Within these herds, the lesions did not show much variability in morphological stages, the majority of which were small creamy grey lesions. No visible lesions were found within any of the 27 herds on the West Coast, so the 63/100 positive herds were all located in Waikato, Manawatu or South Canterbury. In Waikato, 241 cows with visible BDD lesions were detected in 34/40 herds, while in Manawatu, 68 cows with BDD lesions were detected in 15/41 herds, and in South Canterbury, 337 cows with BDD lesions were present in the 14/19 herds. The apparent herd level prevalence and median within-herd prevalences of affected herds across the different regions are summarised in Table 2. The maximum apparent within-herd prevalences were 9.5%, 5% and 6.7% in Waikato, Manawatu and South Canterbury, respectively.

4.5.2. Bayesian inference

Table 3 compares the Bayesian inference of the herd level prevalences τ (under different priors for τ) to the apparent herd level prevalences in the three affected regions. Table 4 summarises, by region and by different priors for τ, the proportion of the sampled herds that were truly affected and the point estimate for τ regarded as a prediction for whether a randomly selected "new" herd would be affected. The posteriors for τ in Waikato and South Canterbury were reasonably robust to changes in the prior for τ, while the posteriors for those in Manawatu were sensitive to the priors (31.9% vs. 43.3% depending on prior). However, the posteriors for the proportion of the sampled herds which were affected in any region were robust

to the prior for τ. By increasing the best prior estimate of sensitivity from 50% to 90%, the posteriors for the herd level prevalences in the three regions hardly changed. They were 59.1% (95% probability interval [PI]: 44.2%-73.8%) in Waikato, 43.2% (95%PI: 29%-58.9%) in Manawatu and 65.7% (95%PI: 49.3%-79.9%) in South Canterbury. By using a pessimistic prior for specificity, the posteriors for the herd level prevalences in the three regions declined moderately. They were 56.2% (95%PI: 41.2%-70.9%) in Waikato, 38.4% (95%PI: 24.9%-54.1%) in Manawatu and 60.9% (95%PI: 44.2%-76.2%) in South Canterbury.

The median within-herd prevalences in Waikato, Manawatu and South Canterbury were estimated as 3.2% (95%PI: 2%-5%), 1.7% (95%PI: 0.9%-3.1%) and 3.7% (95%PI: 2.4%-5.5%) if the prior for τ of beta (10.9, 7.6) was used. These prevalence estimates were not sensitive to the different priors for τ or the sensitivity and specificity of BDD detection. By using a pessimistic specificity, the estimated median within-herd prevalences in Waikato, Manawatu and South Canterbury were fairly robust; i.e. 3.1% (95%PI: 1.9%-5%), 2% (95%PI: 1%-3.6%) and 3.9% (95%PI: 2.5%-5.8%), respectively. The estimated within-herd prevalences also declined slightly in the three regions by increasing the best prior estimate of sensitivity from 50% to 90%. They were 2.7% (95%PI: 1.6%-4.8%) in Waikato, 1.6% (95%PI: 0.8-3.5%) in Manawatu and 3.1% (95%PI: 2%-5.3) in South Canterbury.

For the herds with highest apparent within-herd prevalences in Waikato (9.5%), Manawatu (5%) and South Canterbury (6.7%), their within-herd prevalences were estimated as 13.4%, 7.3% and 10%, respectively. Figure 2a-c display the prevalence distributions for affected herds in the three affected regions. Figure 3 compares the true counts of BDD cows predicted by the model with the observed counts of BDD cows in dairy herds in Waikato (ID 1-40) and South Canterbury (ID

41-59) where BDD infection was more common than Manawatu. Based on the model, herds with one or two cows with visible BDD lesions may have had "zero" true BDD positive cows. This problem was only relevant in Manawatu and Waikato as such low counts were not observed in South Canterbury. The probability of BDD freedom in the West Coast was estimated as 99.97%.

4.6. Discussion

This cross-sectional study investigated the BDD prevalence in four regions of NZ. Combined with the results from Taranaki (Yang et al., 2017a, b), these results provide an overview of BDD distribution in different regions across NZ with different climates, geography and management practices, and show that there are appreciable differences in the herd and cow level prevalence of BDD lesions across the four regions. An investigation of possible risk factors associated with these differences will be performed in the future.

The largest difference was that between the West Coast (where, as of February 2017, the disease appears to be absent) and the other three regions where disease was seen in multiple herds. The reasons the absence of BDD on the West Coast are not clear from this study. However, the first author observed that on the West Coast cows' feet were cleaner than in the other three regions. This may be related to the high rainfall in this region, with the rain washing off the dirt. Foot hygiene is associated with BDD prevalence: the cleaner the feet, the lower the prevalence (Relun et al., 2013a). Another possibility is that the relative isolation of the West Coast (the number of cattle movements into the region is much lower than that of the other 3 regions in this study (Anon, 2018) has resulted in the disease not entering the West Coast at a rate sufficient to persist. .

The apparent herd level prevalence of BDD in Manawatu was much lower than that in Waikato and South Canterbury, and also lower than that reported in Taranaki (Yang et al., 2017b). This was also the case for the estimated true herd level prevalence. Even though that estimate was moderately sensitive to the prior, no matter what prior was used, the true herd level prevalence in Manawatu was lower than in Waikato and South Canterbury (see Table 4). This might indicate potential differences in management practices between regions which could affect herd-to-herd BDD transmission.

The highest apparent herd level prevalence (85%) was recorded in the Waikato; however the estimate of true herd level prevalence was only 59.2%. This was probably because the model predicted "zero" true BDD cases in 10 large herds (the median of numbers of tested animals = 412) where only one or two cases were detected during the visual assessment (see Figure 3). Therefore, the results of the model suggest that care should be taken when classifying large herds as positive for BDD when only one or two cows are identified as having BDD lesions consistent with BDD. This conclusion needs further investigation. This could include using a more sensitive method of lesion detection in such herds (i.e. examination of the lifted foot) , using an additional diagnostic test e.g. histology (Read and Walker, 1998), or using repeated measurements.

The apparent cow level prevalence in affected herds in Manawatu (0.9%), as for the true herd level prevalence, was lower than in Waikato (1.5%), South Canterbury (2.6%) and Taranaki (1.7%, Yang et al., 2017b). The pattern was also seen in the true cow level prevalence (Manawatu at 1.7%, Waikato at 3.2%, Taranaki at 2.9% (Yang et al., 2017a) and South Canterbury (3.7%)). Compared to results from overseas, both the true herd and cow level prevalences seen in this study were lower

than most recent reports from North America and Europe. For example, in Alberta, Canada, Solano et al. (2016) reported that BDD was present on 65/69 (94%) farms and in 15% of cows, while Capion et al. (2008) reported that in Denmark, BDD was present in 47/55 (85%) herds with an average cow level prevalence of 22%. However, in Switzerland, Becker et al. (2014) reported that despite 29.1% of cows having BDD lesions, only 57/78 (73%) dairy herds were affected. This herd level figure is comparable to the NZ situation; for example, for South Canterbury the apparent proportion of affected herds was 73.7% and the true herd level prevalence was 65.9%. This suggests that the risk of BDD transmission between herds may not be much lower in the pasture-based systems of New Zealand than in housing-based systems in North America and Europe, however, within herd transmission (and thus true cow level prevalence) is much lower. The highest true within-herd prevalence seen in this study (13.4%) was lower than the average cow level prevalence recorded in North America and Europe (Capion et al., 2008; Becker et al., 2014; Solano et al., 2016); even though those reports included herds that were free of the disease in their calculation of cow level prevalence. This is probably due to keeping cows at pasture which has been shown to significantly reduce the risk of BDD (Holzhauer et al., 2012). Nevertheless, significant within-herd transmission of BDD can occur in pasture-based herds. In a survey of 13 pasture-based herds in Victoria, Australia, BDD lesions were observed in all herds and mean within-herd prevalence was 19.1% (range 6.2% - 32%), so continued observation of BDD is essential (Coombe et al., 2018).

This study has shown appreciable regional variation in the proportion of affected herds; thus using one region's information as priors for other regions may lead to unreliable estimates. Thus we suggest that if a similar study is undertaken in

other regions of New Zealand that a small scale region-specific herd sample should be undertaken to obtain priors for that region before undertaking large scale sampling. This would avoid the use of the dramatically different priors that we used in this study. This large range of priors was in order to robustly test how sensitive herd level prevalence was to its prior, as we were not sure that the priors from Taranaki were optimal. This sensitivity analysis showed that for two of the three BDD-positive regions, the priors from Taranaki were acceptable.

4.7. Conclusion

The study confirmed that as well being present in Taranaki, BDD was also present in other regions of New Zealand. There were marked differences between regions in the herd and cow-level prevalence of BDD lesions with Manawatu having lower prevalence of disease at both levels than Waikato, South Canterbury, and Taranaki. No disease was seen in West Coast herds, and modelling showed that we were 99.97% sure that the absence of lesions was because BDD was absent from the West Coast.

4.8. Conflict of interest

None to declare.

4.9. Role of the funding source

The first author is funded by the Massey University Doctoral Scholarship. The funding sources had no involvement in the study design, data collection, analyses and interpretations of the data, and the content of and the decision to submit the article for publication.

4.10. Acknowledgements

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4.11. Appendix

In this section, we provide OpenBUGS code for the analyses for Waikato and the West Coast region.

4.11.1. Appendix A: Code for data analysis for Waikato region using the Bayesian superpopulation approach

```
model
{
for (i in 1:40) {
x[i]~dbin(pitilda[i],n[i]) #number of T+ in sampled n
pitilda[i]<-pi[i]*se+(1-pi[i])*(1-sp) #pi is the true superpopulation prev, pitilda is the ap of T+
z[i]~dbern(pI) #the proportion of superpopulations that are affected
pi[i] <- p[i]*z[i] # p is its prev if superpopulation i is affected
logit(p[i]) <- mu + w[i] # model the median of the prev dist using logit-normal
w[i]~dnorm(0, prec)
zx[i] <- step(x[i]-1)  # trick BUGS when x=0
nx[i] <- x[i] + 1 - zx[i]   # x[i] or 1
pvp[i] <-pi[i]*se/pitilda[i]*zx[i]   # positive predictive value
Xplus[i] ~ dbin(pvp[i],nx[i])      #number of true positive among the T+ individual
zn[i] <-step(n[i]-x[i]-1)  # trick BUGS when n-x = 0
nmx[i] <-n[i]-x[i] + 1 - zn[i]   #n-x is T-
pfn[i] <- pi[i]*(1-se)/(1-pitilda[i])*zn[i]  #false negative rate
Xminus[i] ~dbin(pfn[i],nmx[i]) #number of false negative out of T-
X[i] <- Xplus[i]+Xminus[i] #number of disease out of N
pN[i]<- X[i]/n[i] # prev in finite population
pr[i] <-  step(X[i] -1)  # Pr(herd i has inf animals)
}
pih[1] <- sum(pr[])/40      #prop inf herds
#simulating a randomly selected new herd
```

```
for (i in 41:41) {z[i] ~ dbern(pI)
pp[i] <- z[i]*p[i]
XX[i] ~ dbin(pp[i],N[i])
N[i] ~dpois(335) #poisson mean is average herd size
logit(p[i]) <- mu + w[i]
w[i]~dnorm(0, prec)
ppr[i] <- step(XX[i] - 1)  }
#priors
pI ~ dbeta(10.902,7.6013)
#pI~dbeta(3.2618,3.2618) #50, <80
#pI~dbeta(2.3457,4.14)#30,>10
se~dbeta(20.9967,11.7675)
sp~dbeta(88.27996,1.8816)#99,>95
mu<-logit(p0)
p0~dbeta(4.5494,115.7631) #median prev 0.03, <0.07
prec <-1/sigma/sigma
sigma~dunif(0,1)
#prev dist
logit(p00) <- mu +  ww
ww ~ dnorm(0, prec)
}
```

4.11.2. Appendix B: Code for data analysis for the West Coast

```
model{ N <- 12972
  z ~ dbern(pI) #prob of inf in this population
   y ~ dbin(p,N)  #number of T+ in sampled N
   p <- pi*se + (1-pi)*(1- sp) #ap and tp
  pi <- z*prev # prev is its prevalence if the population is affected
#priors
se~dbeta(20.9967,11.7675) #65,>50
sp~dbeta(88.27996,1.8816)#99,>95
prev ~ dbeta(4.5494,115.7631) # 0.03, <0.07
pI ~ dbeta(10.902,7.6013) #60, >40
#predict
future ~ dpois(mupi) #using Pois to approxi binom, future is the count of the BDD
mupi<-pi*n #Pois mean
n<-10000000 #population size
pr<-1-step(future-1) #P(a≥b): step (a-b)
 }
```

4.12. References

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Table 4-1 Estimates of sensitivity, specificity with 95% confidence intervals (CI) or credible intervals (CrI) of visual inspecting bovine digital dermatitis lesions after washing cows' hind feet in milking parlour.

Source	Sensitivity	95%CI/CrI	Specificity	95%CI/CrI
Rodriguez-Lainz et al. (1998)	72%	53%-86%	99%	93%-99%
Thomsen et al. (2008)	65%	59%-72%	84%	81%-87%
Relun et al. (2011)	90%	86%-94%	80%	75%-85%
Yang et al. (2017a)	63.1%	45.1%-78.9%	99.9%	99.8%-99.9%
Cramer et al. (2018)	57.7%	53.2%-62.2%	95.3%	93.3%-96.8%

Table 4-2 Statistics of the herd and cow numbers, apparent herd level prevalence (AHP) with 95% confidence interval (CI) and apparent median within-herd prevalence in affected herds (AMWHP) for bovine digital dermatitis.

	Region			
Parameters	Waikato	Manawatu	The West Coast	South Canterbury
No. of herds	40	41	27	19
No. of cows	15522	15546	12978	15803
No. of affected herds	34	15	0	14
No. of cows in affected herds	13827	6157	0	11544
No. affected cows	241	68	0	337
AHP	85%	36.6%	0	73.7%
95%CI of AHP	70.1%-94.3%	22.1%-53.1%		48.8%-90.9%
AMWHP	1.5%	0.9%	0	2.6%

Table 4-3 Comparing the apparent herd level prevalence (AHP) with the 95% confidence interval (CI) to the Bayesian inference on true herd level prevalence (τ) with the 95% probability interval (PI) for bovine digital dermatitis given different priors for the proportion of the superpopulations being affected.

Parameters	AHP(%) (95%CI)	τ(%) (95%PI)	τ(%) (95%PI)	τ(%) (95%PI)
Regions/Priors		beta (10.9, 7.6)[1]	beta (3.26, 3.26)[2]	beta (2.35, 4.14)[3]
Waikato	85 (70.1-94.3)	59.2 (44.3-73.9)	57.5 (40-75.2)	54.6 (37.4-72.5)
Manawatu	36.6 (22.1-53.1)	43.3 (29-59)	35.2 (20.1-53.5)	31.9 (17.5-49.6)
South Canterbury	73.7 (48.8-90.9)	65.9 (49.5-79.9)	66.9 (46.6-83.4)	63.1 (42.8-80.5)

1: Best estimate 0.6 and 95% sure >0.4

2: Best estimate 0.5 and 95% sure <0.8

3: Best estimate 0.3 and 95% sure >0.1

Table 4-4 Comparing the true proportion of the sampled herds being bovine digital dermatitis affected (TPS) to the predicted probability of a randomly selected "new" herd being affected (PPR) under different priors for the proportion of the superpopulations being affected.

Region	Parameter	Prior		
		beta (10.9, 7.6)[1]	beta (3.26, 3.26)[2]	beta (2.35, 4.14)[3]
Waikato	TPS	58%	57.5%	56.5%
	PPR	58.4%	56.8%	54.2%
Manawatu	TPS	33.7%	31.5%	30.3%
	PPR	42.1%	34.6%	31.7%
South Canterbury	TPS	72%	72%	71.8%
	PPR	65.5%	66.2%	62.6%

1: Best estimate 0.6 and 95% sure >0.4

2: Best estimate 0.5 and 95% sure <0.8

3: Best estimate 0.3 and 95% sure >0.1

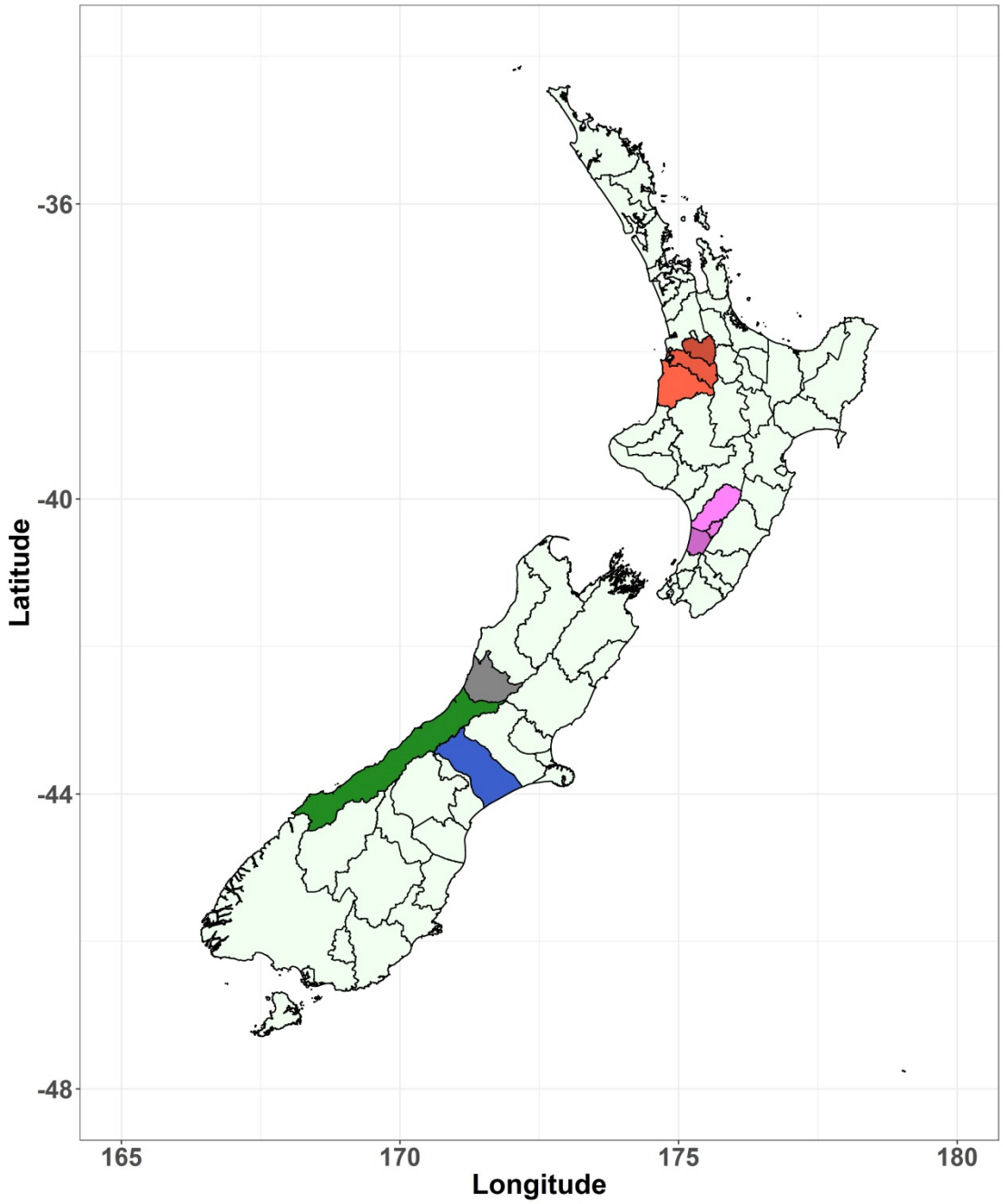
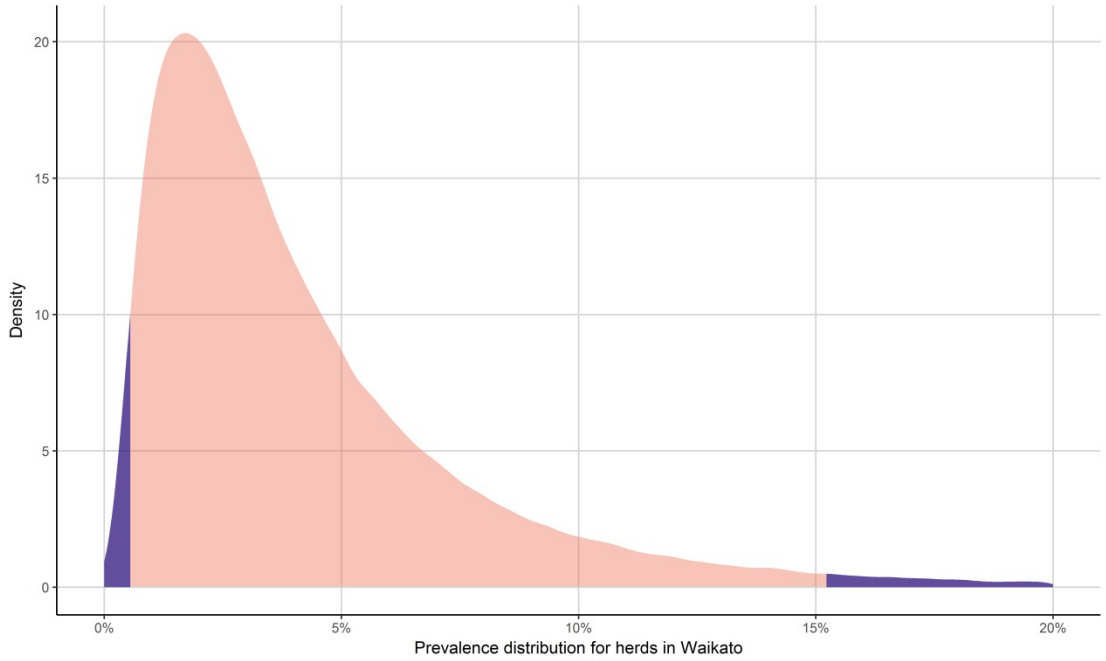
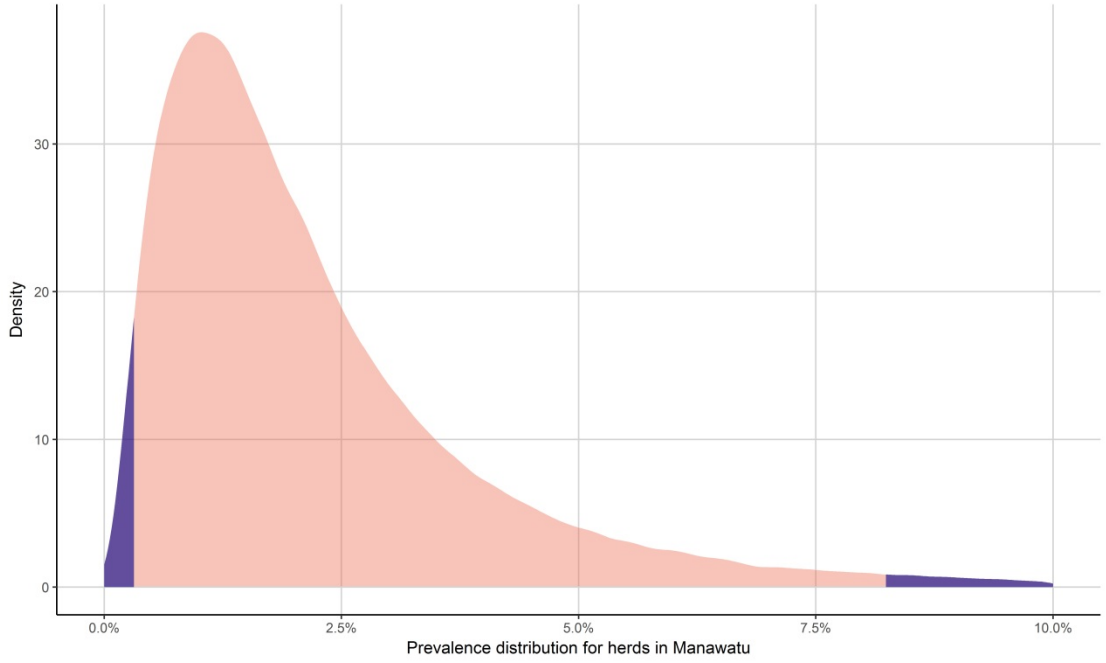


Figure 4-1 Sampled areas for bovine digital dermatitis in New Zealand; shaded areas in red are sampled areas in Waikato, shaded areas in orchid are sampled areas in Manawatu, shaded area in grey and green are sampled areas of Greymouth and Westland, respectively on the West Coast, and shaded area in blue is South Canterbury.


Density
20
15
10
5
0
0%
5%
10%
15%
20%
Prevalence distribution for herds in Waikato


Density
30
20
10
0
0.0%
2.5%
5.0%
7.5%
10.0%
Prevalence distribution for herds in Manawatu

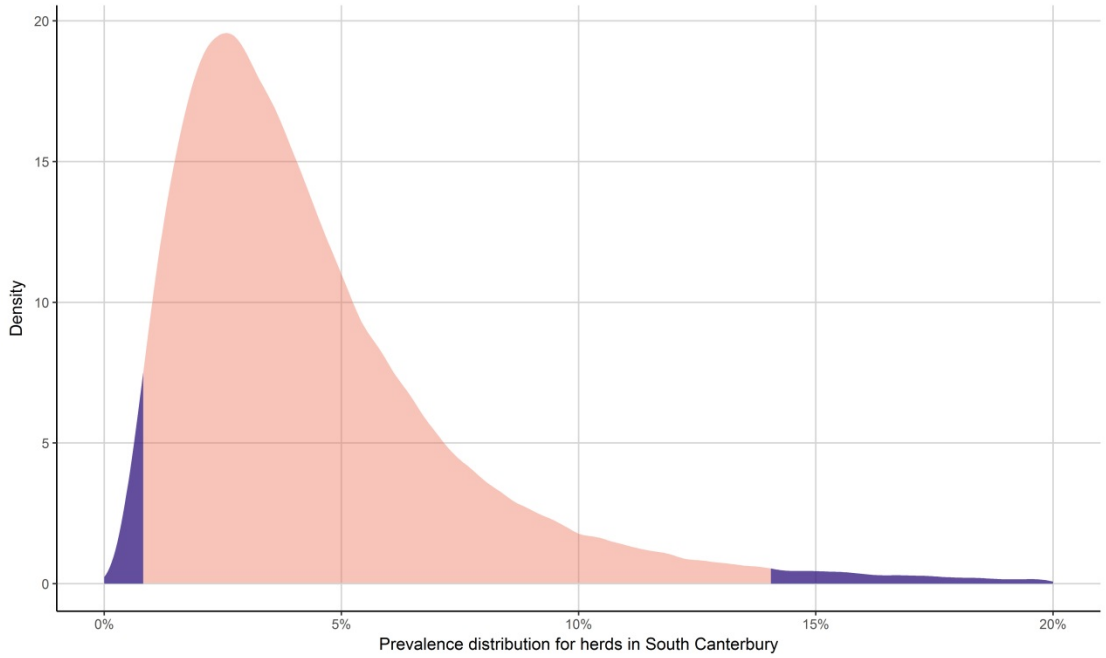


Figure 4-2 Prevalence distribution estimates for within-herd prevalence in Waikato, Manawatu and South Canterbury. The blue shaded areas are out of 95% high density interval.

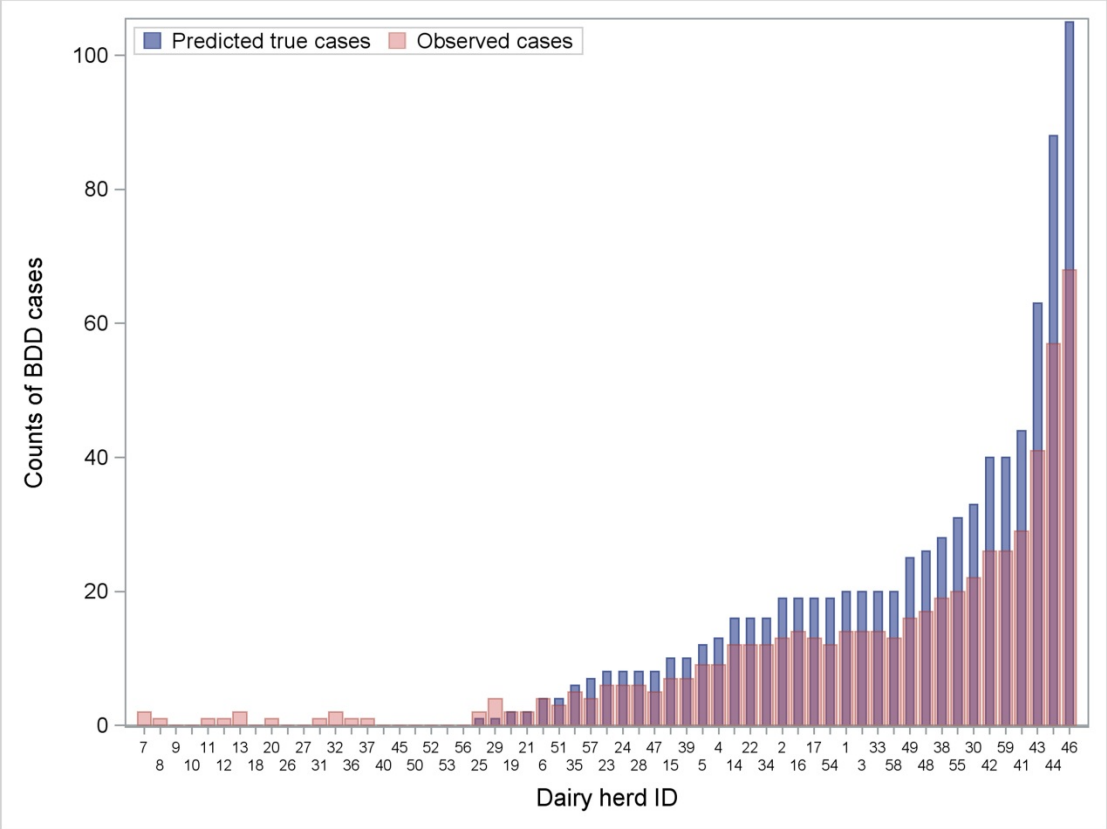


Figure 4-3 Comparing the true numbers of digital dermatitis (BDD) cases predicted by the Bayesian superpopulation model to the observed numbers of cows with BDD in dairy herds in Waikato (ID 1-40) and South Canterbury (ID 41-59), the predicted numbers of cases took the observed positive/negative counts into account and made an adjustment (using the model) accounting for false positive and negative recordings of observed positive/negative decisions.

Chapter 5. Bayesian analysis of herd-level risk factors for bovine digital dermatitis in New Zealand dairy herds

This chapter is prepared in the style format of BMC Veterinary Research. The published manuscript is presented in appendix.

5.1. Abstract

5.1.1. Background

Bovine digital dermatitis (BDD) is considered the most important infectious cause of lameness in dairy cattle worldwide, but has only recently been observed in New Zealand. Although many studies have investigated the risk factors for BDD in confined dairy systems, information on risk factors in pasture-based system is limited. Therefore a cross-sectional study including 59,849 animals from 127 dairy herds in four regions of New Zealand was conducted to identify the herd-level factors associated with the probability of a herd being BDD-lesion positive and with within-herd BDD prevalence.

5.1.2. Results

Purchasing heifers was associated with increased odds of a herd being BDD-lesion positive (odds ratio [OR]: 2.33, 95% probability interval [PI]: 1.26-4.42) and a cow being BDD affected (OR: 3.76, 95%PI: 1.73-8.38), respectively. Higher odds of a herd being BDD-lesion positive (OR: 2.06, 95%PI: 1.17-3.62) and a cow being BDD affected (OR: 2.87, 95%PI: 1.43-5.94) were also seen in herds where heifers co-grazed with cattle from other properties. In addition, using outside staff to treat lameness was associated with higher odds of a cow being BDD affected (OR: 2.18, 95%PI: 0.96-4.98).

5.1.3. Conclusion

This study highlighted that movements of heifers are significantly associated with the spread of BDD within and between dairy herds in New Zealand. To minimise the risk of disease introductions in herds where moving heifers cannot be avoided, it

is best to purchase heifers only from herds where BDD-freedom has been confirmed and, if heifers have to graze-off a farm, they should be reared as a single biosecure management group, especially since animals may be BDD-infected without having clinically obvious lesions.

5.2. Keywords

Digital dermatitis, Dairy cattle, Lameness, Risk factors, Pastoral system, Bayesian, Multilevel modelling

5.3. Background

Bovine digital dermatitis (BDD) has been found throughout the world in both confined and pasture-based dairy systems [1, 2]. In many countries, BDD appears to be endemic in dairy herds [3] and is commonly considered as the most important infectious cause of cattle lameness [4]. Clinically, BDD lesions progress or regress through different morphological stages, commonly described using M scores [5, 6]. A rapid BDD lesion detection method such as visual examination during milking is widely used in many studies [7]; although interpretation of such diagnostic outcome is subjective, which usually requires additional validation studies to assess the agreement across the examiners [8].

Multiple studies have evaluated the risk factors associated with BDD prevalence within herds in confined dairy systems. These studies have identified a wide-range of potential risk factors including type of housing [9], using outside staff to trim hooves [10], footbath regimen [11] and access to pasture [12]. In contrast, very few studies [13-15] have been undertaken in cattle that are principally pasture-based with no or very limited use of housing, where many of the risk factors identified in confined animals are irrelevant. Specific research in such systems is essential as there can be large variation between pasture-based dairy herds in the prevalence of BDD [16].

In New Zealand, one previous study has evaluated herd-level risk factors for BDD, but that was undertaken in only one region [14]. In that study we used a Bayesian hurdle model to explore the associations between risk factors and BDD prevalence at both the herd and animal levels. The initial separation of the herds into BDD-lesion-free and BDD-lesion positive was based on whether BDD lesions were observed; i.e. a herd with ≥1 lesion was defined as being BDD-lesion positive,

otherwise it was defined as being BDD-lesion free [14]. However, simply basing herd status on the presence/absence of visible lesions probably leads to loss of information regarding probability of a herd having BDD and may introduce misclassification bias at the herd level, as there is a chance that a herd where BDD lesions are truly present could be wrongly classified as being BDD-lesion-free due to a combination of limited diagnostic sensitivity and low cow-level prevalence [17].

One method for overcoming this limitation is by using a Bayesian latent class model, which estimates the mean probability of a herd being BDD-lesion positive conditional on the number of test positive animals, the total number of animals tested, and the test characteristics [17]. Thus, the mean probability contains more precise information than the simple dichotomised outcome and increases the power of the study to determine the impact of risk factors on the likelihood of a herd being BDD-lesion positive.

The aim of this study was to use Bayesian methods to investigate the impact of farm management practices on pasture-based dairy herds across New Zealand on 1) the probability of a herd being BDD-lesion positive obtained from a previous Bayesian latent class analysis [16] and 2) the within-herd BDD prevalence, namely the probability of a cow within a herd having BDD lesions.

5.4. Methods

5.4.1. Target and source population

The target population was the pasture-based dairy herds in New Zealand and the source population was the herds in the four regions across New Zealand: Waikato and Manawatu in the North Island and the West Coast and Canterbury in the South Island. These regions encompass most of the dairy systems (all grass fed and self-

contained; feed imported, either supplement or grazing-off and feed imported to extend lactation) used in New Zealand [16].

5.4.2. Data collection

The dataset was collected as described by Yang et al. [16]. Briefly, the data collection started in the Waikato and moved south following the seasonal pattern of calving to ensure that the great majority of the herds were milking at the herd examinations. In the first phase, half the sampled herds were visited in each region before moving on to the next. In the second phase, the order was reversed, starting in Canterbury and going back north. Within each herd, visual assessment was performed on cows' rear feet in the milking parlour after hosing the feet gently [7].

The farm management practices undertaken in the previous 12 months were collected alongside the visual inspection for BDD using a questionnaire given to the owners or managers of the study herds. The questionnaire was modified by the authors from that used in Yang et al. [14]. The questionnaires were answered after the herd inspection while the first author was still on the farm, so that if the owners or managers were unsure of a question, the first author could explain the intent of the question. The categorical management predictors collected via the questionnaire are shown in Table 1 and a copy of the questionnaire is provided as an additional file [see Additional file 1].

5.4.3. Data processing

The data were imported into Stata 13.1 for cleaning and analysis (StataCorp, USA). One-way tables were used to examine the frequency of responses for each level within the categorical variables. Levels with low frequencies were combined

with adjacent levels where biologically plausible. As hoof trimmers were rarely used to trim cows or treat lame cows, this level was combined with using vets to treat lame cows, to create a new dichotomous variable of whether or not the farm had outside staff trimming cows or treating lame cows. Since few farmers reported chemically disinfecting hoof trimming equipment, "chemical disinfection" and "washed by water" were combined to create a new variable of whether or not trimming equipment was cleaned between animals. Since few farmers reported purchasing dairy heifers or cows from saleyards, "saleyards" was combined with "other farms", to create new variables of whether heifers and cows were purchased from outside. Similarly, cow houses were rarely used, so "cow house" was combined with "stand-off pad" and a new variable was created to describe whether the cows were permanently pasture-based (except for milking) or not. All categorical variables included in the final analysis had at least two levels and each level had at least ≥ 15% of the total responses for the question.

5.4.4. Evaluating seasonal variation

As this was a cross-sectional study, the impact of season on BDD-lesion status and lesion prevalence was not of primary interest. However, as all the data were collected by the first author, it was not possible to complete the data collection in a short time frame and therefore herds were sampled at different points throughout the 2016/2017 lactation season. To confirm that BDD-lesion status and lesion prevalence did not vary significantly between different months, generalized estimating equations [18] and beta regression models were respectively used to examine whether the average cow-level prevalence or probabilities of a herd being BDD-lesion positive differed significantly between months in Waikato and Manawatu regions. This

process was not applied to Canterbury since 18/19 herds were visited in the same month.

5.4.5. Univariable models

For the two outcome variables (within-herd prevalence and probability of a herd being BDD-lesion positive), univariable logistic regression models and univariable beta regression models in the frequentist framework were respectively used to select predictors for fitting in the multivariable models. Any predictors with p-value ≤ 0.2 were included in the further analyses.

5.4.6. Multivariable model 1

This analysis was designed to quantify the strength of associations between farm management practices and within-herd prevalence. A Bayesian binomial model was constructed. The model was built using a forward stepwise strategy. The predictors were retained in the model when the 90% probability intervals of their corresponding regression coefficients did not overlap 0. If inclusion of a predictor altered the coefficient of any of the existing predictors by > 15%; the newly included predictor was considered as a confounder and was forced into the model regardless its 90% probability interval [19]. Once the preliminary main effect model was constructed, two-way interactions between all predictors in the model were created. An interaction term was retained if its 95% probability interval excluded 0. The final model structure is presented below:

$$y_j \sim binomial\left(p_j, n_j\right)$$

$$\text{logit}\left(p_j\right) = \beta_0 + \beta_1 x_j + \beta_2 g_j + \beta_3 h_j + U_{region(j)} + W_j \quad (1)$$

$$U_{region(j)} \sim N(0, \sigma_U)$$

$$W_j \sim N(0, \sigma_W)$$

where y_j was the number of the cows with visible BDD lesions in the j^{th} herd of all the regions, which was modelled using a binomial distribution with the parameters: the proportion of cows with visible lesions (p_j) and number of cows being examined (n_j); β_0 was the intercept, β_1, β_2 and β_3 were the regression coefficients for the predictors x_j, g_j and h_j which represented whether heifers were purchased from outside sources, whether heifers were co-grazed with heifers from other farms and whether outside personnel treated lame cows. Finally, $U_{region(j)}$, W_j were the random effects at regional and herd level, respectively and modelled using two independent normal distributions with zero means and standard deviations σ_U and σ_W.

The choice of prior distributions contributes to the posterior distributions, thus utilising informative priors results in better inferences compared to "vague" priors [20]. It is difficult to place informative priors for the regression coefficients. However, such priors can be indirectly induced to define probabilities for different combinations of predictors. Partially informative priors were assigned to β_0, β_1 and β_2. First, the proportion of cows with visible lesions (prevalence) in a "typical" closed herd was defined as $\tilde{p}_0$. This meant $x = 0$, $g = 0$ and $h = 0$. Therefore, according to equation 1, $\beta_0 = \text{logit}\left(\tilde{p}_0\right)$. Second, specify $\tilde{p}_1$ as the prevalence of a herd where some heifers were purchased from outside, in this case, $x = 1$, but $g = 0$ and $h = 0$. Thus, $\beta_1 = \text{logit}\left(\tilde{p}_1\right) - \beta_0$. Finally, let $\tilde{p}_2$ denote the prevalence of a herd which contained purchased heifers, and, at the same time, sent its own heifers to co-graze

with heifers from other farms ($x = 1$ and $g = 1$, but $h = 0$). This gave $\beta_2 = \text{logit}(\tilde{p}_2) - \text{logit}(\tilde{p}_1)$. Logit-normal distribution was used for these prevalence priors. Below we use $\tilde{p}_0$ as an example to illustrate the way to convert a prevalence estimate to its corresponding logit-normal distribution such as $\text{logit}(\tilde{p}_0) \sim N(\mu_{\beta 0}, \tau_{\beta 0})$, where τ is the precision term defined as the reciprocal of the variance. Our best estimate of the prevalence in a closed herd was m_0 and we were 95% confident that it was less than l_0; then $\mu_{\beta 0} = \text{logit}(m_0)$. The standard deviation $\sigma_{\beta 0} = [\text{logit}(l_0) - \text{logit}(m_0)]/1.645$, eventually $\tau_{\beta 0} = 1/\sigma_{\beta 0}^2$.

The best estimates of $\tilde{p}_0$, $\tilde{p}_1$ and $\tilde{p}_2$ came from the previous analyses of BDD data in Taranaki and the authors' expert opinion. One important observation was that in contrast to previous studies of housed cattle, the apparent cow-level prevalence of BDD was very low (mean = 1.2%, Yang et al. [1]) with 26.8% of herds having fewer than1% of cows with observed lesions. In Canterbury region, where median herd size was 840 and >21% of herds had ≥ 1000 cows; we were able to detect BDD at an apparent within-herd prevalence of 0.1% (i.e. one cow with lesions in a 1000-cow herd). Thus to reflect our belief that a closed herd was likely to have no or extremely rare BDD lesions, we took 0.05% as our "best point estimate" for $\tilde{p}_0$. Furthermore we were also 95% confident that it was less than 0.35%, i.e., one cow with BDD lesion(s) in a 300-cow herd. Based on the method described in the last paragraph, this led to $\mu_{\beta 0} = -7.6$ and $\tau_{\beta 0} = 0.71$. Table 2 summarises our "best estimates" for $\tilde{p}_0$, $\tilde{p}_1$ and $\tilde{p}_2$. Uniform priors (0, 3) and (0, 2) were set for σ_U and σ_W, respectively. This reflected our belief that the variability of herd-level prevalence across regions was bigger than the variability across herds. However, the parameter values assigned to the uniform priors were considered to be non-specific as we did not know the standard deviations of the two random effects.

Under the partially informative priors, the fit of the model to the data was evaluated using posterior predictive checks which compared the observed outcome data to the data simulated/predicted by the posterior predictive distribution [21]. The Bayesian P-value quantifies the probability that the discrepancy between the predicted and observed values. A Bayesian P-value close to 0.50 indicates adequate model fit, although a value between 0.20 and 0.80 is also accepted [22].

Sensitivity analysis was used to assess the sensitivity of the posteriors to the priors. Table 3 summarises the distributions of the model priors and the priors used for the sensitivity analysis. The model was developed using OpenBUGS [23]. Posterior inferences were obtained using Markov chain Monte Carlo (MCMC) approximation. The posterior distribution of each parameter was reported using median and 95% probability interval (PI). After discarding the first 10 000 iterations as burn-in period, the model was further run for 100 000 iterations. Convergence was assessed using BGR-plots by running three chains with different sets of initial values [24].

5.4.7. Multivariable model 2

This analysis was designed to assess the associations between farm management predictors and the probability of herd being BDD-lesion positive (PP). This analysis did not include herds on the West Coast as the region was determined to be free of the disease [16].

The data were modelled using a Bayesian beta model [25]. π_k was used to denote the PP_k for k^{th} herd . The variable "region" was initially modelled as a random effect $V_{region(k)} \sim N(0, \frac{1}{\sqrt{\tau_V}})$, where τ_V was the precision term. The model was constructed as follows:

$$\pi_k \sim Beta\ (a_k, b_k)$$

$$a_k = \mu_k \varphi \quad (2)$$

$$b_k = \varphi(1 - \mu_k) \quad (3)$$

$$\text{logit}(\mu_k) = \gamma z_k + V_{region(k)} \quad (4)$$

$$V_{region(k)} \sim N(0, \frac{1}{\sqrt{\tau}_V})$$

where z_k was the predictor vector, γ denoted the regression coefficient vector and μ_k the mean and φ a measure of variability, with a larger value of φ indicating less variability [26].

Diffuse normal distributions (mean = 0, precision = 0.01) were set for all the regression coefficients, and a vague gamma distribution (1, 1) was set for φ and τ_V. The model was built using a forward stepwise strategy. Predictors were retained if the 90% probability interval for the regression coefficients excluded 0. Confounders were assessed using the method described as per Multivariable model 1. Two-way interactions between all predictors in model were investigated after building the main effect model. Inclusion criteria for an interaction term were the same as for Multivariable model 1. In this model, the linear predictor was the log-odds. The odds were defined as the probability of a herd being BDD-lesion positive divided by the probability of a herd being BDD-lesion-negative at each level of a predictor. The model was therefore able to identify any farm management practice associated with higher odds of being BDD-lesion positive for a randomly selected herd in any BDD-affected region.

5.4.8. Multivariable model 3

Although the mixed effects beta model modelled the overall variability of the probability in different regions; it was not able to describe the difference between particular regions, therefore we also built a model which treated "region" as a fixed effect. Assuming the model had in total *t* farm management practices, equation (4) was changed to:

$$\text{logit}(\mu_k) = \gamma_c z_{ck} + \gamma_w z_{wk} + \gamma_1 z_{1k} + \cdots + \gamma_t z_{tk} \quad (5)$$

with $V_{region(k)} \sim N\left(0, \frac{1}{\sqrt{\tau}_V}\right)$ dropped. Here, z_{ck} and z_{wk} were the dummy variables for the regions Canterbury and Waikato (level "Manawatu" was treated as reference level). This fixed effects model can be used to predict the probability of a herd being BDD-lesion positive with different covariates in any particular region.

The deviance information criteria (DIC) of both beta models were compared. In addition, a global measure of variation explained by each of the beta models was obtained by computing pseudo-R^2 defined as the squared correlation between the linear predictor and the logit-transformed outcome variable [27]. Both beta models were developed using OpenBUGS [23]. After discarding the first 5000 iterations as the burn-in period, the model was further run for 100 000 iterations. Convergence was assessed using BGR-plots by running three chains with different sets of initial values [24]. The OpenBUGS code for Multivariable model 1, 2 and 3 is provided as an additional file [see Additional file 2].

5.5. Results

There was no evidence to support seasonal differences in any of the outcome variables. In Waikato region, the average cow-level prevalences in September 2016 and in January 2017 were not significantly different (P = 0.94). The probabilities of

BDD-lesion positive also did not differ significantly between these two months (P = 0.65). In Manawatu, the average cow-level prevalences in September (P = 0.46) and November (P = 0.22) were not significantly different to that in December. Similarly, significant differences in the probabilities of BDD-lesion positive in September (P = 0.86), November (P = 0.28) and December were not evident. These findings ruled out the potential seasonal impact on BDD prevalences in this study. Table 4 displays the total herds and animals sampled as well as the proportions of herds/animals having BDD lesions in each region during the data collecting period.

The outputs from the Bayesian binomial model (Multivariable model 1) with our partially informative priors are shown in Table 5. Lack of model fit was not evident (Bayesian P-value = 0.5). The posteriors for β_1, β_2 and β_3 were robust in all sensitivity analysis scenarios. The posterior median for β_0 increased slightly (-8.05 vs. -7.67) and its 95%PI was also wider (-10.65, -5.707) given the diffuse prior *N* (-5, 0.001) rather than the informative prior. The posterior for σ_W was not sensitive to its prior, although the posterior for σ_U was sensitive to its prior. The posterior median of σ_U increased from 2.4 to 3.2 when the prior changed from Uniform (0, 3) to Uniform (0, 5). It further increased to 4 if the prior changed to Uniform (0, 9). Nevertheless, there was no impact on the posteriors for the regression coefficients. The results of the sensitivity analyses are provided as an additional file [see Additional file 3].

Based on Multivariable model 1, cattle in a herd which purchased heifers from outside were more likely to have BDD lesions than cattle in a herd that did not purchase heifers (OR: 3.76, 95%PI: 1.73-8.38). Being in a herd which co-grazed heifers with animals from other properties also increased the odds of a cow having BDD lesions (OR: 2.87, 95%PI: 1.43-5.94). The use of outside staff to treat lameness

was found to be associated with the increased within-herd prevalence (OR: 2.18, 95%PI: 0.96-4.98).

Except for the intercepts, the posteriors for the parameters reported by the Bayesian mixed effects beta model and fixed effects beta model were nearly identical. Table 6 summarises the models' outputs. The DIC for each model was also very similar, -533.3 for the fixed effects model and -533.5 for the mixed effects model. Two farm management practices were identified as being significantly associated with the odds of a herd being BDD-lesion positive. Based on the mixed effects beta model, the odds of a herd being BDD-lesion positive was 2.33 times (95%PI: 1.26-4.42) higher in a herd with purchased heifers compared to one without, and 2.06 times (95%PI: 1.17-3.62) higher if heifers co-grazed with cattle from other properties. The predicted probabilities from the fixed effects model of a herd being BDD-lesion positive conditional on different farm management practices and region are displayed in Figure 1. However, 74% of the variation in the probability of a herd being BDD-lesion positive remained unexplained by either beta model (pseudo-$R^2 = 0.26$).

5.6. Discussion

This study found that both co-grazing with heifers from other properties and purchasing heifers from other farms were associated with an increased probability of a herd being BDD-lesion positive as well as increased within-herd prevalence. Our previous study [14] also found that that youngstock movement between farms considerably increased the probability of a farm having at least one visible lesion (OR: 4.15, 95%PI: 1.39-15.27). Compared to Yang et al. [14], our current study evaluated youngstock movement in a more detailed way by dividing such movements into heifer purchasing and heifer co-grazing. Unlike Yang et al. [14] who reported

that youngstock movement affected only a herd's probability of having at least one cow with BDD lesions but not within-herd prevalence, this broader-scale study (along with the more detailed way of recording the predictors) found that youngstock movement increased both the probability of a herd being BDD-lesion positive and the within-herd prevalence. The likely inference is that heifers act as a reservoir for BDD transmission between dairy herds and between cows within herds in New Zealand [28]. In contrast, both this analysis and Yang et al. [14] found no effect of purchasing adult cattle on BDD risk. This lack of effect is most likely due to the much smaller numbers of purchased adult cows compared to the numbers of heifers purchased for replacement [13, 14].

Yang et al. [14] reported that herds with a rotary platform were more likely to have at least one cow with BDD lesions than herds with a herringbone (OR: 3.19, 95%PI: 1.31-8.51), though as with heifer movement, no effect was seen on within-herd prevalence. This may have been due to the ease of finding at least one lesion in herds with rotary platforms rather than being an actual risk factor [14]. Our current analysis did not include parlour type in the final model as the analysis found it to be neither statistically significant nor a confounder.

Two New Zealand studies [14, 15] reported that on BDD-positive farms, the within-herd prevalence was higher on farms where the outside staff came for hoof trimming (prevalence ratio [PR]: 3.13, 95%PI: 1.25-7.29 and risk ratio [RR]: 2.06, 95% confidence interval [CI]: 1.05-4.06). Although our current analysis did not confirm this finding, the calculated OR 2.18 was still in the realm considered to be biologically important [10] and the 95%PI: 0.96-4.98 only just included 1. It is not entirely clear how these effects could be mediated under New Zealand conditions. The use of outside staff for lame cows is typically unrelated to BDD since BDD rarely

causes lameness in New Zealand dairy cattle. However, failure to clean trimming equipment properly between cows and between herds could represent a mechanism for spread [14]. To confirm this hypothesis, our current study included whether trimming equipment was cleaned between cows as a potential risk factor. However, no effect of cleaning/washing equipment between cows was found; this suggests that if there is an effect of outside staff on the within-herd prevalence of BDD that it is not mediated via dirty equipment. Further research is required to better estimate the impact of using outside staff to treat lame cows on BDD prevalence and to investigate potential pathways by which such an effect could be mediated.

The only other study of risk factors for BDD in pasture-based cows is that by Rodriguez-Lainz et al. [13]. However, of the 22 farms in that study only 2 kept their cattle at pasture all year round, with 13/22 keeping cattle in an open corral or loose yard for at least part of the year, whereas in this study, all 127 farms grazed their cattle throughout the year. As such many of the factors analysed by Rodriguez-Lainz et al. [13] (e.g. housing type and season of calving) are not directly relevant to the New Zealand situation and thus not included in our analysis. Although it is difficult to directly compare the study findings, Rodriguez-Lainz et al. [13] did find that there was an effect of purchasing replacement heifers on within-herd prevalence of BDD (OR: 3.16, 95%CI: 1.61-6.21), but not purchasing adult cows (OR: 1.31, 95%CI: 0.72-2.38). The data from Rodriguez-Lainz et al. [13] provided no evidence as to whether, in pasture-based cattle, using outside staff to trim feet increases the within-herd prevalence of BDD as in that study all cattle were treated or trimmed by farm staff. However, using hoof trimmers who operated on multiple farms was found to be significantly associated with higher BDD within-herd incidence in housed cattle (OR: 2.8, 95%CI: 1.9-4.2) [10].

Many studies on dairy cattle from intensive housing systems in the northern hemisphere have also identified herd-level risk factors for this disease. Decreasing the access to pasture was found to increase the risk of BDD [12, 29, 30]. The type of housing for animals was also associated with BDD prevalence, i.e. cows that housed in cubicles had higher BDD prevalence and more severe BDD cases [31] than cows in straw yards, which also agreed with Onyiro et al. [9]. In cubicles houses, the size of cubicles was linked to the risk of BDD [29]. This is because cows tend to spend longer time standing in shorter and narrower cubicles; therefore the contact between heels and slurry was increased [32]. However, these factors tend not to be an issue in New Zealand pasture-based systems and were therefore not included in the current study. It could be interesting in future studies to evaluate cleanliness of legs in cattle since higher prevalence of BDD had been found in cows with dirty legs [33]. This is one possible explanation why no BDD lesions were seen on the West Coast where the cows' feet were generally much cleaner compared to other regions.

The results of this study show that even in New Zealand where BDD prevalence is very low, heifers are the most likely source of disease spread between and within herds. Particular care should be taken when purchasing heifers as replacement animals and ideally, replacement heifers should only be purchased from herds where BDD-freedom has been confirmed. The latter may be difficult in New Zealand since many heifers are purchased in late-autumn when cows are not being milked and it is therefore not possible to observe the milking herd for BDD. In such cases, visual inspection of the whole heifer group (not just the heifers for purchase) is a potential alternative to increase the probability of finding at least one animal with BDD lesions. If any of the heifers have visible lesion(s), then the entire group should not be purchased as animals can still be infected with BDD in the absence of visible

lesions [34]. Where heifers are co-grazing with animals from multiple herds, it becomes much more difficult to ensure that co-grazing heifers will not come in contact with BDD infected cattle, although little is currently known about the transmission dynamics of BDD in grazed dry stock. Thus, the only reliable method to ensure that heifers grazed away from the farm do not become infected with BDD is to require that they are grazed as a single biosecure management group. This is important to prevent the spread of many infectious diseases as well as BDD.

Bayesian methods were adopted as the analytical approach in this paper. Bayesian analyses incorporate previous scientific understanding, e.g. such as the likely association between a farm management practice and BDD within-herd prevalence, into analysis (see Multivariable model 1), so that the inference (i.e. the posterior distribution) is based on both the data and our prior information. This is in contrast to other methods which typically ignore such previous understanding [35]. Furthermore even if previous information of a research question is not available, the Bayesian methods still has significant advantages such as being able to directly compare the relative probabilities of two or more hypotheses rather than simply using the probability of the data given the null hypothesis to determine whether an alternative hypothesis was plausible.

Multivariable model 2 and 3 used uniform priors, as this was the first use of beta models to study risk factors on the herd-level BDD outcome estimated from a previous Bayesian latent class analysis. This use of the outcome from the latent class analysis reduced the likelihood of misclassification errors at the herd level, as the effect of diagnostic sensitivity and specificity on the herd level diagnosis was factored into the latent class model [16].

Although misclassification bias has been adjusted at the herd level in Multivariable model 2 and 3, our Multivariable model 1 did not account for animal level misclassifications. This could potentially have influenced the analysis of risk factors affecting within-herd prevalence. Misclassification at the individual level, as at the herd level, can be minimised by incorporating the known sensitivity and specificity of a diagnostic method [36]. However, when the impact of specificity and sensitivity on the diagnosis of BDD in the individual animal was included during the modelling process, it resulted in non-convergence of the Markov chains. This may be related to the model being non-identifiable. Using a more sensitive detection method inspecting lifted cows' feet in the trimming chute, would have decreased any potential impact but would have been cost prohibitive [7].

The other limitation was that Multivariable models 2 and 3 explained only 26% of the variation in the probability of a herd being BDD-positive. This indicates that further investigation of more factors which could potentially affect the probability of herd being BDD-lesion positive was required.

5.7. Conclusions

Our study investigated potential risk factors for BDD across New Zealand and identified that purchasing replacement heifers and co-grazing heifers with animals from other herds were significantly associated with a higher probability of a herd being BDD-lesion positive and higher within-herd prevalence of BDD. This is consistent with previous findings from pasture-based systems. However, the identified risk factors only explained a small proportion of the variation in probability of a herd being BDD-lesion positive. Our study also found that using outside staff for trimming had a large effect on within-herd prevalence (doubling the odds of an individual cow

having BDD). Given that we can't rule out the possibility of contaminated hoof trimming equipment contributing to the between-herd spread of BDD, it would be advisable for farms to maintain their own set of equipment. Further research should be undertaken to better estimate the impact of this factor on BDD and how it can be mediated through different biosecurity interventions.

5.8. List of abbreviations

BDD: Bovine digital dermatitis; **PI:** Probability interval; **CI:** Confidence interval; **PR:** Prevalence ratio; **RR:** Risk ratio; **OR:** Odds ratio; **MCMC:** Markov chain Monte Carlo; **PP:** Probability of herd being BDD-lesion positive; **DIC:** Deviance information criteria

5.9. Declarations

5.9.1. Ethics approval and consent to participate

The New Zealand Animal Welfare Act (1999) states that if an animal is subject to a manipulation, it needs ethics approval.

Section three of this act defines a manipulation as follows:

In this Act, unless the context otherwise requires, the term manipulation, in relation to an animal, means, subject to subsections (1A) to (3), interfering with the normal physiological, behavioural, or anatomical integrity of the animal by deliberately—

(a) subjecting it to a procedure which is unusual or abnormal when compared with that to which animals of that type would be subjected under normal management or practice and which involves—

(i) exposing the animal to any parasite, micro-organism, drug, chemical, biological product, radiation, electrical stimulation, or environmental condition; or

(ii) enforced activity, restraint, nutrition, or surgical intervention; or

(b) depriving the animal of usual care;—

As washing of feet to observe BDD is normal management and the animals were observed during milking (so there is no restraint beyond normal) what was done does not meet the definition of a manipulation.

5.9.2. Permission from farm owners

The farm owners were identified by local veterinary practices and verbal agreement was obtained prior to visiting farms.

5.9.3. Consent for publication

Not applicable.

5.9.4. Availability of data and material

The subset of the data was available in additional file 2. The full data collected and analysed during the current study are not publicly available as they contain confidential information of the participated farmers. However, the datasets are available from the corresponding author on reasonable request.

5.9.5. Competing interests

The authors declare that they have no competing interests.

5.9.6. Funding

The first author is funded by the Massey University Doctoral Scholarship. The funding source had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.

5.9.7. Authors' contributions

DAY, KRM and RAL participated in the study design and coordination. DAY collected the data and analysed the data. DAY, MCG and RAL contributed to the manuscript. All authors were involved in the manuscript preparation and approved the final manuscript.

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5.9.9. Authors' information

Dr Yang obtained his bachelor's degree in veterinary medicine and a master's degree in vet epidemiology; he is working towards his PhD in vet science.

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Additional files (See Appendix 4)

Additional file 1: The questionnaire used to collect farm management practices.

(DOCX 177 kb)

Additional file 2: OpenBUGS code for the three Bayesian multivariable models used in this study. (DOCX 20 kb)

Additional file 3: Results of the sensitivity analysis for Multivariable model 1.

(DOCX 19 kb)

Table 5-1 Herd-level predictors on BDD collected from 127 New Zealand dairy herds.

Variable	Levels	Herds with BDD lesions N (%)	Herds without BDD lesions N (%)	Total
Type of milking parlour	Rotary	29 (51%)	28 (49%)	57
	Herringbone	34 (49%)	36 (51%)	70
Calving season	Spring only	57 (49%)	59 (51%)	116
	Spring and Autumn	6 (55%)	5 (45%)	11
Whether or not having dairy cattle milking on more than one farm	Yes	9 (14%)	6 (9%)	15
	No	54 (48%)	58 (52%)	112
Source of acquired adult cows (>2 years old)	Other farms	8 (62%)	5 (38%)	13
	Saleyard	2 (50%)	2 (50%)	4
	Not acquiring	53 (48%)	57 (52%)	110
Source of acquired bulls	Other farms	36 (47%)	41 (53%)	77
	Saleyard	9 (64%)	5 (36%)	14
	Not acquiring	18 (50%)	18 (50%)	36
Source of acquired heifers	Other farms	15 (68%)	7 (32%)	22
	Saleyard	1 (50%)	1 (50%)	2
	Not acquiring	47 (46%)	56 (54%)	103
Whether your calves/heifers co-grazing with calves/heifers from other farms	Yes	46 (59%)	32 (41%)	78
	No	17 (35%)	32 (65%)	49
Whether your milking dairy cattle co-grazing with cows from other farms in winter	Yes	28 (57%)	21 (43%)	49
	No	35 (45%)	43 (55%)	78
Providing grazing for stock from other farms at your farm or not	Yes	3 (50%)	3 (50%)	6
	No	60 (50%)	61 (50%)	121
Using a transport company to transport animals (not for slaughter) or not	Yes	43 (49%)	45 (51%)	88
	No	20 (51%)	19 (49%)	39
Share a loading ramp or not	Yes	7 (41%)	10 (59%)	17
	No	56 (51%)	54 (49%)	110

Who did most of the hoof trimming/ lame cattle treatment on your farm	Vet	7 (39%)	11 (61%)	18
	Hoof trimmer	6 (86%)	1 (14%)	7
	On-farm staff	50 (49%)	52 (51%)	102
Trimming equipment cleaning methods	Washed by water	28 (51%)	27 (49%)	55
	Chemically disinfected	11 (55%)	9 (45%)	20
	Not wash	24 (46%)	28 (54%)	52
Use a footbath or not	Yes	10 (63%)	6 (37%)	16
	No	53 (48%)	58 (52%)	111
Whether or not use stand-off pads or cow houses in winter or poor weather	Stand-off pad	18 (49%)	19 (51%)	37
	Cow house	2 (22%)	7 (78%)	9
	Neither	43 (53%)	38 (47%)	81
Main material of the walking track/race from paddock to the milking parlour	Gravel	22 (35%)	40 (65%)	62
	Concrete	1 (50%)	1 (50%)	2
	Other	40 (63%)	23 (37%)	63
Use feedpad or not	Yes	23 (48%)	25 (52%)	48
	No	40 (51%)	39 (49%)	79

BDD, bovine digital dermatitis; N (%), numbers of herds having such a predictor (row percentage of herds having such a predictor)
Average herd milk solid production in BDD-lesion positive/negative herds were 414.9 kg/cow year and 414.1 kg/cow year, respectively

Table 5-2 The "best estimates" for within-herd prevalence ($\tilde{\boldsymbol{p}}_{\boldsymbol{k}}$) of BDD conditional on the different covariates.

			Prevalence	
	Purchasing heifers	Heifers co-grazing	prior mode	95th percentile
$\tilde{p}_0$	No	No	0.05%	0.35%
$\tilde{p}_1$	Yes	No	0.2%	1%
$\tilde{p}_2$	Yes	Yes	0.5%	3%

BDD, bovine digital dermatitis

Table 5-3 The prior distributions for parameters used in the Bayesian multilevel multivariable binomial model.

Parameter	**Main analysis**	**Sensitivity analysis scenarios**		
		1	2	3
β_0	N (-7.6, 0.71)	N (-5, 0.001)	N (-7.6, 0.71)	N (-7.6, 0.71)
β_1	$\text{logit}(\tilde{p}_1) - \beta_0$	N (0, 0.001)	$\text{logit}(\tilde{p}_1) - \beta_0$	$\text{logit}(\tilde{p}_1) - \beta_0$
β_2	$\text{logit}(\tilde{p}_2) - \text{logit}(\tilde{p}_1)$	N (0, 0.001)	$\text{logit}(\tilde{p}_2) - \text{logit}(\tilde{p}_1)$	$\text{logit}(\tilde{p}_2) - \text{logit}(\tilde{p}_1)$
β_3	N (0, 0.001)	N (0, 0.001)	N (0, 0.001)	N (0, 0.001)
σ_U	Uniform (0, 3)	Uniform (0, 3)	Uniform (0, 5)	Uniform (0, 9)
σ_W	Uniform (0, 2)	Uniform (0, 2)	Uniform (0, 3)	Uniform (0, 2)

β_0, intercept; β_1, purchasing heifers; β_2, heifers co-grazing; β_3, lameness treated by outside staff
σ_U and σ_W, standard deviation of random effects at region and herd levels
$\tilde{p}_1$ ~ logit-normal (-6.21, 1.03); $\tilde{p}_2$ ~ logit-normal (-5.29, 0.82)

Table 5-4 Total (#) herds/cattle sampled, proportions (%) of herds/cattle with BDD lesions detected in each region.

	Region			
Parameters	Waikato	Manawatu	The West Coast	South Canterbury
# of herds	40	41	27	19
# and % of affected herds	34 (85%)	15 (37%)	0	14 (74%)
# of cows	15522	15546	12978	15803
# and % affected cows	241 (1.6%)	68 (0.4%)	0	337 (2.1%)

BDD, bovine digital dermatitis

Table 5-5 The posterior distributions for parameters of the Bayesian multilevel multivariable binomial model.

Parameter	**Interpretation**	**Posterior distribution**		
		Median	2.5th Percentile	97.5th Percentile
β_0	Intercept	-7.67	-8.9	-6.46
β_1	Purchasing heifers	1.32	0.55	2.13
β_2	Heifers co-grazing	1.06	0.36	1.78
β_3	Lameness treated by outside staff	0.78	-0.04	1.61
σ_U	Region level random effect	2.36	1.33	2.97
σ_W	Herd level random effect	1.41	1.12	1.8

Table 5-6 The posterior distributions for parameters of the Bayesian beta models.

Parameter		Posterior distribution		
		Median	2.5th Percentile	97.5th Percentile
	Mixed effects beta model			
γ_0	Intercept	0.07	-1.13	1.36
γ_1	Heifers co-grazing	0.73	0.16	1.29
γ_2	Purchasing heifers	0.85	0.23	1.49
φ		0.53	0.42	0.66
τ_V		1.43	0.22	4.81
	Fixed effects beta model			
γ_0	Intercept	-0.38	-0.93	0.16
γ_1	Heifers co-grazing	0.72	0.15	1.28
γ_2	Purchasing heifers	0.84	0.22	1.48
γ_c	Canterbury	0.82	0.11	1.55
γ_w	Waikato	0.50	-0.08	1.09
φ		0.53	0.42	0.66

$\varphi = a + b$, where a and b are shape parameters of a beta distribution
τ_V, precision term of the region level random effect defined as 1/variance

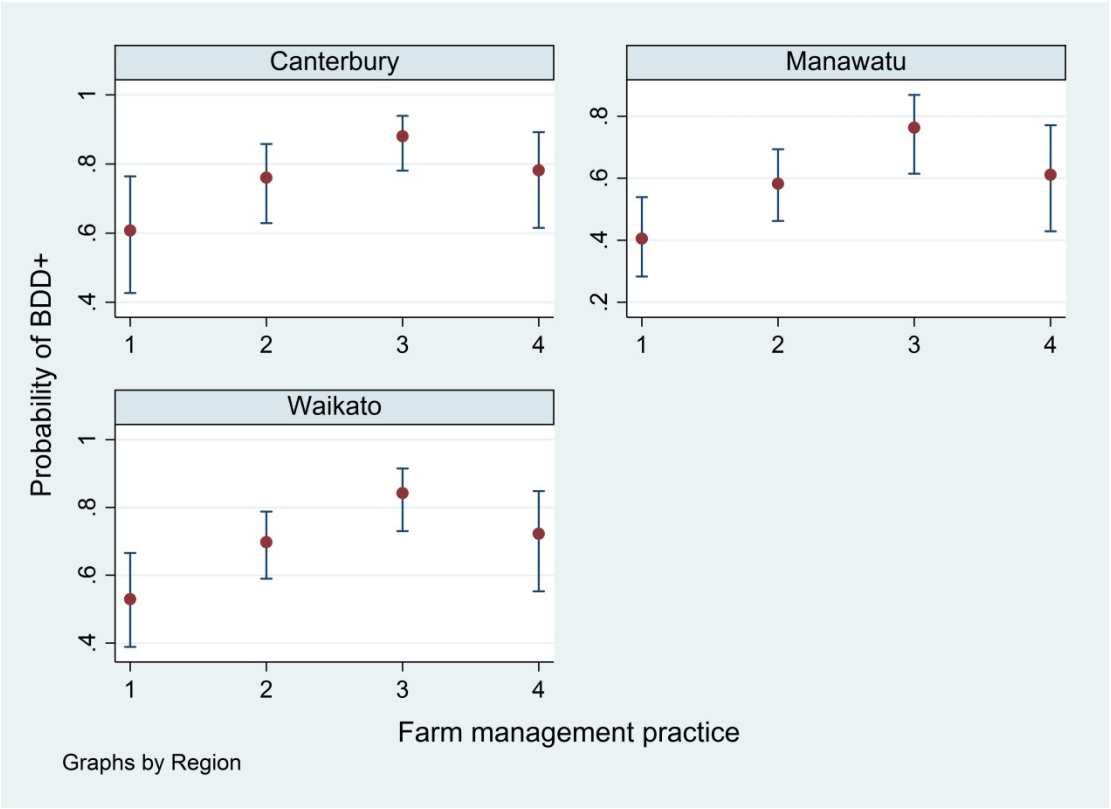

Figure 5-1 Predicted probability of a herd being BDD-lesion positive given different farm management practices. 1 = a closed herd, 2 = a herd having heifers co-grazing with animals from other properties only, 3 = a herd having heifers co-grazing with animals from other properties and having purchased heifers, 4 = a herd having purchased heifers only; BDD = bovine digital dermatitis.

Chapter 6. Modelling the infection dynamics of bovine digital dermatitis in New Zealand pastoral dairy production systems

This chapter is prepared in the style format of Veterinary Research.

6.1. Abstract

Bovine digital dermatitis (DD) is an important infectious cause of cattle lameness worldwide that has become increasingly prevalent in New Zealand pastoral dairy herds. In this study, a modified DD lesion development model based on simplified Iowa DD scoring system was applied to explore the transmission dynamics of DD in a typical spring-calving pastoral New Zealand dairy herd. The modified model only included three compartments: normal skin, early stage and advanced lesions. Lesions regressing after treatment were excluded as DD lesions are rarely treated in New Zealand. Furthermore, sub-classes within each lesion class were not defined due to the lack of variability in DD lesion presentations within New Zealand.

The model was validated based on longitudinal field data from three dairy herds in the Waikato region during one lactation season (2017-18). The model suggested that in infected dairy herds, although DD prevalence will tend to increase year-on-year it is likely to remain relatively low (<18%) even after 10 years of within-herd transmission. It is likely that the low transmission rate during the late lactation (model assumption) results in more cases resolving than developing during this period and therefore results in the low prevalence of infectious cattle at the start of each subsequent lactation. Cattle with advanced lesions had a stronger influence on the establishment and maintenance of DD than cattle with early stage lesions highlighting the importance of targeting these animals for intervention. On-going monitoring of DD is highly recommended to assess the long-term progression of the disease in affected dairy herds.

6.2. Keywords

Digital dermatitis, Dairy cattle, Lameness, Modelling, Transmission

6.3. Introduction

Bovine digital dermatitis (DD) is an infectious foot disease that causes varying levels of pain, discomfort, and lameness in dairy cattle [1] and has been increasingly found in cattle production systems worldwide [2,3]. In countries where cows are housed indoors, DD can be a major infectious cause of cattle lameness as well as a significant problem for the dairy industry due to losses in milk production [4], increased treatment costs [5], and negative impacts on animal welfare [6]. Once established in a herd, DD typically becomes endemic and very few herds are able to completely eradicate the disease [7] due to the multifactorial and complex interactions between the bacteria [8], animal [9] and environment [10].

In pasture-based systems, such as those that predominate in New Zealand, DD lesions are typically less commonly seen than in housed cattle [11]. As this lower prevalence of cattle with visible lesions is combined with a decreased likelihood that an animal with lesions will be lame [12], under New Zealand conditions it is likely that DD will have only limited impacts on herd-level production [13]. However, routine monitoring of DD is still recommended to identify early cases of the disease and to make sure DD remains manageable at the herd level [14].

From an epidemiological perspective, recording the different morphological stages of DD lesions in cattle is also important as it provides insights into the pathophysiology of the disease [15] and its transmission dynamics at the population level [16]. The most widely used classification system for DD lesions is the “M score” scheme developed by Döpfer et al. [17] and extended by Berry et al. [18]. The description of each M score is summarised in Table 1.

Two previous studies [16,19] have built mathematical simulation models to explore the lesion transition dynamics of DD in a housed cow setting. Döpfer et al. [16] adopted an SEIS structure to describe the lesions transitions in a large, closed population of dairy cattle. They assumed that class M0 was the susceptible class (S), that classes M1 and M3 were latently infected or exposed (E) and that classes M2 and M4 were infectious (I). The model restricted the potential transitions between stages (e.g. M2 could be moved in from both M1 and M4, but could only move out to M3 and M3 could not move back to M2). In contrast, Biemans et al. [19] considered that all classes except M0 were infectious, and adopted the SIS structure to study the relative contributions of different M classes to DD transmission. They did not restrict the potential transitions between stages. Döpfer et al. [16] identified that the speed of identifying acute lesions (M2) and the effectiveness of treating these lesions were the keys to DD control. In contrast, Biemans et al. [19] concluded that M4 lesions made the greatest contribution to disease transmission and that control should be focused on lowering the number of M4 lesions.

Although these models provide valuable insights, model frameworks based on M scores are difficult to implement in New Zealand dairy herds due to differences in DD lesion presentations and the limitations of DD inspection during milking. Most affected cattle in New Zealand have M4-like lesions. These are typically small grey, rubbery, lesions which may or may not have thickened, darker edges. Less commonly larger, more proliferative lesions can also be found. Red active (M2) lesions are extremely rare [20]. Post-treatment M3 lesions are not a feature of the disease in New Zealand as lesions are treated only very rarely. Herd size and lack of suitable facilities

means that on most farms the only feasible method of DD detection is observation during milking, ruling out accurate identification of M1 and M4.1 stages [21].

Thus there is a need to explore different classification schemes when creating transmission models that are designed to be applied to pastoral-based production systems. One alternative to the "M scores" scheme, is the Iowa DD scoring system [22]. DD lesions in New Zealand can be at least partially described using that system, i.e. the small grey rubbery lesions have a similar presentation to the type A pre-clinical lesions; while the large proliferative lesions could be regarded as clinical lesions [22]. However, classification needs to be simplified to fit New Zealand conditions. In particular, the lack of variability in lesion presentations means that sub-classes within pre-clinical and clinical lesions are not likely to be useful and as discussed earlier neither are regressing post-treatment lesions.

The aim of this study was to use the simplified Iowa DD lesion scoring system to explore the transmission dynamics of DD under New Zealand pastoral production systems. The validity of the simplified model was assessed by comparing the model output with the longitudinal field data collected from DD affected herds across a single lactation. The implications for disease control based on the model findings are also discussed.

6.4. Material and methods

6.4.1. Field data

Longitudinal data on lesion occurrence and type were collected over a single lactation season in three spring-calving herds in the Waikato region of New Zealand.

The herds had all been previously identified as having DD from a previous cross-sectional study [20] and were selected on a convenience basis since they were located close together, the farmers were willing to have repeated visits from the researcher, and the farmers agreed not to use DD treatments during the study (unless there was a significant welfare concern for the animal). The herds were intended to be visited weekly by the first author over the 36 week period from 21th August 2017 to 30th April 2018. However, due to scheduling conflicts, a total of 19 observation weeks were available for Herd 1, 16 observation weeks for Herd 2, and 17 observation weeks for Herd 3.

Each herd visit was timed during the day to coincide with routine milking. The rear feet of all milking cows were hosed as necessary to remove mud and faecal contamination before being examined with an aid of a hand torch to identify DD lesions [23]. The maximum numbers of cows examined at a milking were 286, 194, and 273 for Herd 1, Herd 2 and Herd 3, respectively. The timetable of the herd visits is provided as an additional file [see Additional file 1].

6.4.2. Simulation model

A simple deterministic compartmental model was then developed to capture the transmission dynamics of DD in a typical spring-calving pastoral New Zealand dairy herd. This included a demographic component and disease component as described below.

6.4.3. Herd demographics

A simplified herd demographic structure was modelled based on the typical annual management calendar of a spring-calving dairy herd in New Zealand. The start

of lactation was set to 1st Aug and lasted 285 days until the fixed herd dry-off date of 12th May the following year. Culling was modelled using a simplified assumption that 20% of the cows would be culled on a single day towards the end of lactation (set on 23th April). The dry period lasted from 13th May to 31th July. After 31th July, a new lactation season started and the replacement animals joined the herd on the first day of lactation. The replacement rate was set to be equal to the culling rate (20%) to make sure the herd size remained constant over time. The above process was repeated for each year until the end of the simulation.

6.4.4. Disease dynamics

The types of lesions were described using a simplified Iowa DD scoring system. This is summarised in Figure 1 and includes early stage lesion and advanced lesion. The transitions between these two DD lesion types is described in Figure 2 which is the simplified DD lesion development model where compartment for regressing lesions after treatment was excluded [22]. A susceptible animal (S) was assumed to get infected at a transmission rate β. Once infected, the animal could develop an early stage lesion (I) that was assumed to persist for an average of certain days leading to a transition rate out of the compartment of α – the reciprocal of the persistence duration, before regressing to a susceptible state. Alternatively, an early stage lesion might progress to an advanced lesion (C) with a probability θ and an advanced lesion would persist. Additional assumption was made that both lesion types were infectious and had the same infectivity.

It was assumed that there was homogeneous mixing of individual cows and a constant group size. This meant that the transmission coefficient (β), the product of

the contact rate between animals and the probability of the contact leading to infection, was the same for all susceptible animals [24]. Disease transmission was assumed to be most rapid in early lactation [25]. Therefore, β was time-dependent, such that $\beta_t = \beta_{t-1} - \delta$, where δ reflected the difference between the transmission coefficients between day t and day $t+1$ during the lactation, and was assumed to be constant. The probability that the contacts were with infectious animals (p) was modelled as a frequency-dependent transmission, $\frac{\mathrm{I+C}}{\mathrm{N}}$ [24], where N was the total number of cows in the population.

In the deterministic form, changes in the number of animals in each compartment were modelled using the following equations:

$$\mathrm{S}_t = \mathrm{S}_{t-1} - \frac{\beta_{t-1}\mathrm{S}_{t-1}(\mathrm{I}_{t-1} + \mathrm{C}_{t-1})}{\mathrm{N}_{t-1}} + \alpha \mathrm{I}_{t-1}(1-\theta), \quad (1)$$

$$\mathrm{I}_t = \mathrm{I}_{t-1} + \frac{\beta_{t-1}\mathrm{S}_{t-1}(\mathrm{I}_{t-1} + \mathrm{C}_{t-1})}{\mathrm{N}_{t-1}} - \alpha \mathrm{I}_{t-1}, \quad (2)$$

$$\mathrm{C}_t = C + \alpha \mathrm{I}_{t-1}\theta. \quad (3)$$

6.4.5. Model validation and calibration

The structure of the simulation model was firstly validated by comparing with the field observation data. During the data collection, transitions between normal skin and early stage lesions were frequently observed, which agreed with the model. We also observed no transitions from the only advanced lesion recorded in this study, and its size and appearance did not change appreciably between observations. These observations suggest, in agreement with the model that the advanced lesion may represent a chronic form of DD in New Zealand dairy cattle. However, we did not observe any transitions to an advanced lesion. This is consistent with the findings of

Krull et al. [22] in relation to early stage lesions. We therefore assumed that the advanced lesion observed developed before the beginning of data collection and was preceded by an early stage lesion [22].

As far as the authors' are aware, the DD lesion classification system developed in Iowa [22] has not previously been used for simulation modelling purposes, therefore, no references are available to provide estimates for the parameters required in such model. Hence, initial parameter values were estimated based on the authors' opinion or field observations from New Zealand. The value for the transmission coefficient for the first day of lactation (β_{t_0}) was initially set to be 0.055 as our best estimate. Since we assumed the transmission rate decreased over time by a fixed constant, we initially set $\delta = 0.0002$. The transition rate (α) moving from an early stage lesion to other compartments was the reciprocal of the average persistence of an early stage lesion, which was approximately 7 weeks (49 days) based on field observations. The probability (θ) that an early stage lesion would progress to an advanced lesion was expected to be extremely low, however the exact value was difficult to determine. To be conservative, we used a small value of 0.2% for θ and be carried out a sensitivity analysis to assess the impact of different values of θ on the model output.

Additional calibration of the values for β_{t_0}, α and δ was performed by comparing the seasonal pattern predicted by the simulation model with the field data. The field data were analysed using the following steps: first, the scatter plot of observed prevalence of DD in the three herds against time was plotted. Based on the plot, a generalised linear mixed model (GLMM) treating "herd" as a random effect

and time (X) and X^2 as fixed effects were constructed with a binomial distribution and logit link function. The variance of the random effect was extremely small, confirming the homogeneity of the herds. The model was therefore re-constructed using a generalised linear model (GLM) with a binomial distribution and logit link function. This process was performed using Stata 13 (StataCorp, USA). Based on the estimated regression coefficients, a fitted curve was obtained to compare the field data to the predicted prevalence curve from the simulation model so that the fit of the simulation model could be visually assessed. To ensure a good fit, the values for β_{t_0}, α and δ were manually calibrated until the predicted curve from the simulation model aligned with the fitted curve by the GLM. Table 2 summarises the parameters required in the model and their corresponding values.

6.4.6. Simulation conditions

The calibrated simulation model was then used to explore the transmission dynamics of DD in a population of dairy cows in New Zealand over a period of 10 years. The time step of the model was one day. To capture the low prevalence of DD lesions observed in the field, the herd size needed to be large and was therefore set at 1000. For the first model, a single animal with an advanced lesion was assumed to be in the population at the beginning of the simulation representing a chronically infected animal introduced at the start of the first lactation. The total animals in the population of each simulation day were monitored to make sure the demographics stabilised. The primary outputs of the model were: the long term seasonal pattern of disease, including the timing and the level of the peak prevalence in each year.

Three other initial scenarios were modelled to establish whether the early stage or advanced lesions contributed more to the establishment of DD on New Zealand dairy farms: 1) one animal with an advanced lesion and one animal with an early stage lesion; 2) one animal with an early stage lesion; and 3) two animals with early stage lesions at the beginning of the first lactation.

6.4.7. Sensitivity analysis

A sensitivity analysis was carried out to examine the impact of changing α and θ on the simulation outputs. The sensitivity analysis scenarios are summarised in Table 3.

6.4.8. Statistical analysis

The simulation outputs with each initial infection conditions were plotted against time for a ten year period. The peak prevalences reached during each of those 10 years were summarised for each of the four scenarios. For the scenarios where the advanced lesion was absent at the beginning, the year that the first advanced lesion was observed was identified.

6.5. Results

6.5.1. Model validation

As shown in Figure 3, there was close agreement between the simulation model and field data indicating adequate model fit. In the 2017-2018 lactation seasons, the peak prevalence was 2.7% on 11th January 2018.

6.5.2. DD dynamics

Based on the model predictions, given the presence of one advanced lesion at the start of lactation, DD prevalence would increase to a peak in mid-lactation and then decrease during the late lactation and dry periods. However, DD prevalence at the start of each subsequent season would be higher than that of the previous season. Thus DD prevalence will increase year-on-year. The dynamics of DD at the herd level were different depending on whether an advanced or an early stage lesion was assumed to be present at the beginning of the first lactation of the modelling period. As per Figure 4, if an advanced lesion was found in the first year, DD prevalence would continue to increase in the subsequent 10 years (sub-plots: a & b). However, if advanced lesions were absent at the beginning of the lactation in the first year (sub-plots: c & d), then DD prevalence declined in the second year and remained at a similar level in the third year before starting to increase from the fourth year.

In addition to the impact on the dynamics of DD, the different lesion types also had different effects on the establishment of DD in a herd. By comparing sub-plot “a” to “b” of Figure 4, it was clear that given the existence of an advanced lesion at the beginning of the first lactation, the presence of early stage lesions did not speed up DD transmission. After 10 years, the peak prevalences of the two different initial infection scenarios were 17.2% and 17.9%, respectively. If there were no advanced lesions at the beginning of the first lactation of the 10-year modelling period (sub-plots: c & d of Figure 4), then DD prevalence would only go up to 7% over 10 years if one early stage lesion was found at the beginning of the first lactation, and 10% if two lesions were found.

The number of early stage lesions at the beginning of the first lactation of the modelling period influenced the speed of establishment of the first advanced lesion in the herd. The model suggested that it would take almost nine years to develop the first advanced lesion if there was only one early stage lesion found at the beginning of the first lactation, whereas the first advanced lesion was seen in early lactation in the sixth year if two early stage lesions were found at the beginning of the first lactation.

6.5.3. Sensitivity analysis

The results of the sensitivity analysis are displayed in Figure 5. Increasing or decreasing the infectious duration of the early stage lesion (α) by a week (7 days) both had obvious influences on the simulation model's output (sub-plot a & b). In contrast, altering the probability of an early stage lesion progressing to an advanced lesion (θ) had minimum impact on the simulation outputs, the model still had reasonably good fit if θ was changed to 0.3% or 0.1% (sub-plot c & d).

6.6. Discussion

The simplified DD lesion development model was validated and calibrated based on longitudinal field observations from three herds during the 2017-2018 lactation season. According to the model, the prevalence of DD in affected herds was predicted to remain relatively low even after 10 years of within-herd transmission. This, according to the model, is most likely to because the transmission parameter decreases after peak lactation, which results in a more lesions resolving than developing during the late lactation and dry period, thereby reducing the infection burden in the at the start of the following lacttaion. This is consistent with data from non-pasture-based systems where dry cows are at lower risk of having DD than

lactating cows [26-28]. The model suggests that on New Zealand dairy farms which have DD, the low within-herd prevalence of DD is likely to persist for many years, making it uneconomic for farmers to implement control measures such as routine footbaths which are commonly used to control BDD in housed cattle [29,30]. However the model did suggest that disease prevalence was likely to continue to increase year-on-year. Therefore, we recommend that on infected farms, New Zealand dairy farmers should undertake on-going monitoring of DD to assess the progress of the disease. Ideally, monitoring should occur multiple times during the season as part of routine foot health and lameness assessments [31]. However, if farmers can only conduct DD monitoring at a single time point, the model results suggest that late November to end of February would perhaps be the optimal time as the DD prevalence is likely to reach its peak during this period. This suggestion is consistent with the seasonality seen in a previous New Zealand-based longitudinal study [32].

During the monitoring process, it is important for observers to differentiate between the different lesion types as the relative prevalence of cattle with early stage and advanced lesions can change the transmission dynamics, in particular the speed of increase of peak prevalence. The model predicts that if advanced lesions are present in only 0.1% of cattle then in 10 years' time the prevalence of DD will be ~ 17% whereas if that 0.1% has only early stage lesions then the equivalent figure will be 7%. Thus the model results highlight the potential importance of advanced lesions in the establishment of DD in New Zealand dairy herds. Nevertheless, early stage lesions cannot be ignored completely as increasing the number of early stage lesions present at the start of the modelling period decreases the time prior to the development of the

first advanced lesion, thereby increasing the peak prevalence of DD seen 10 years later.

Advanced lesions are very rare in New Zealand. So far, out of 1353 DD affected cows detected by the first author over the years, four "advanced lesions" including the one found in this study have been observed [11,20]. The other three which are morphologically similar to the advanced lesion found in this study were only observed once in cross-sectional studies and no further observations were made on those three. The photos of the other three "advanced lesions" are provided as an additional file [see Additional file 2]. Thus we lack data on the factors that determine the proportion of lesions which become advanced lesions. However, North American experience suggests that three key factors influence the progression from an early stage lesion to an advanced lesion: 1) presence of necessary bacterial agents, 2) cattle genetics and immunity, and 3) environment [22,33]. Further research is needed to establish whether these key factors are important in the development of advanced lesions in New Zealand pastoral dairy herds.

This study clearly demonstrated that a simplified DD lesion development model could accurately describe lesion progression and regression in the natural condition in New Zealand dairy herds. The simplified Iowa DD scoring system used in the development of this model would be relatively simple for veterinary technicians or farmers to implement. However, further research is needed to confirm the within- and between-observer repeatability of this system [34-36].

As with any simulation model, there are limitations that may affect interpretation of the results. Firstly, we were unable to generate precise estimates for the average length of time cows spent in each lesion state because it was not possible to observe animals more frequently than once per week and, due to schedule conflicts, the time period between consecutive observations was sometimes longer. This is important as there was a relatively large impact of changing the values for α in the sensitivity analysis. In future studies, it may be beneficial to perform more intensive observations in affected herds by using multiple observers, though this will require validation of the scoring system and on-going training [21,36]. Secondly, this model adopted simplified herd demographics without considering the calving and culling patterns in the three herds. This could affect the within-herd transmission dynamics if, for example, in the future, cows with DD lesions are more likely to be culled. Future studies should collect these data along with the DD lesion data.

6.7. Declaration

6.7.1. Abbreviations

DD: digital dermatitis; GLMM: generalised linear mixed model; GLM: generalised linear model

6.7.2. Ethics approval and consent to participate

The New Zealand Animal Welfare Act (1999) states that if an animal is subject to a manipulation, it needs ethics approval.

Section three of this act defines a manipulation as follows:

In this Act, unless the context otherwise requires, the term manipulation, in relation to an animal, means, subject to subsections (1A) to (3), interfering with the normal physiological, behavioural, or anatomical integrity of the animal by deliberately—

(a) subjecting it to a procedure which is unusual or abnormal when compared with that to which animals of that type would be subjected under normal management or practice and which involves—

(i) exposing the animal to any parasite, micro-organism, drug, chemical, biological product, radiation, electrical stimulation, or environmental condition; or

(ii) enforced activity, restraint, nutrition, or surgical intervention; or

(b) depriving the animal of usual care;—

As washing of feet to observe BDD is normal management and the animals were observed during milking (so there is no restraint beyond normal) what was done does not meet the definition of a manipulation.

6.7.3. Consent for publication

Not applicable.

6.7.4. Availability of data and material

The data collected in the current study are not publicly available as they contain confidential information of the participated farmers. However, the datasets are available from the corresponding author on reasonable request.

6.7.5. Competing interests

The authors declare that they have no competing interests.

6.7.6. Funding

The first author is funded by the Massey University Doctoral Scholarship. The funding source had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.

6.7.7. Authors' contributions

DAY, KRM and RAL participated in the study design and coordination. DAY collected the data and analysed the data. DAY and MCG built and validated the simulation model. DAY, MCG and RAL contributed to the manuscript. All authors were involved in the manuscript preparation and approved the final manuscript.

6.7.8. Acknowledgement

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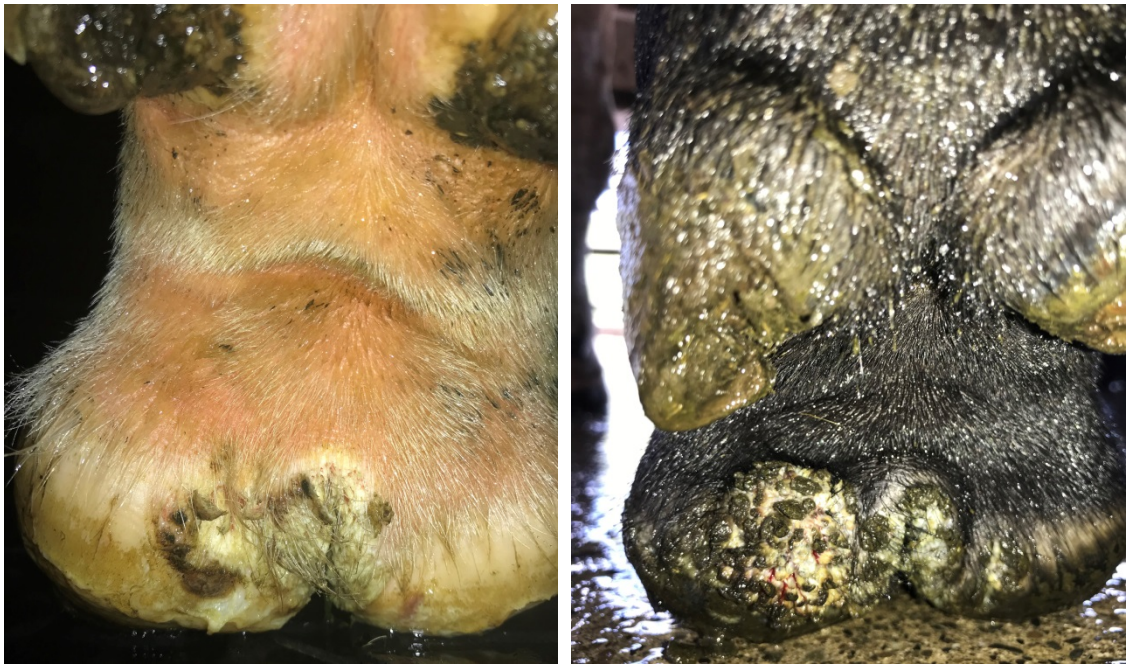

Figure 6-1 Early (left) and advanced (right) DD lesions observed in New Zealand dairy herds. DD = bovine digital dermatitis.

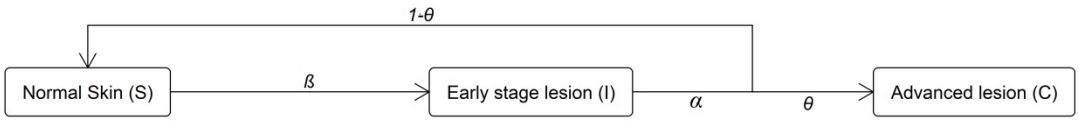

Figure 6-2 Simplified digital dermatitis lesion development model based on Krull et al. (2016). β: transmission coefficient, α: the reciprocal of the average time that early stage lesions persist, θ: probability that an early stage lesions progresses to an advanced lesion

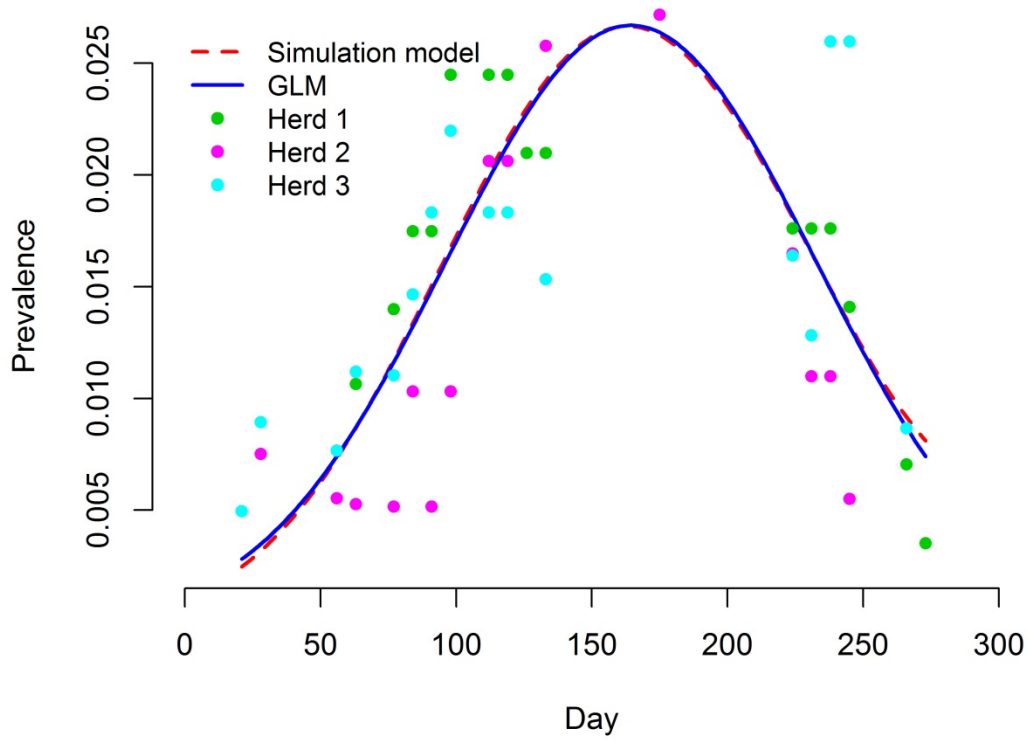

Figure 6-3 Comparing the simulation model output to the field observations. The simulation model is valid as its predicted seasonal pattern (red dashed curve) agrees with the fitted seasonal pattern (blue solid curve) from the filed data collected in three New Zealand dairy herds in 2017-18 lactation season using the generalised linear model (GLM).

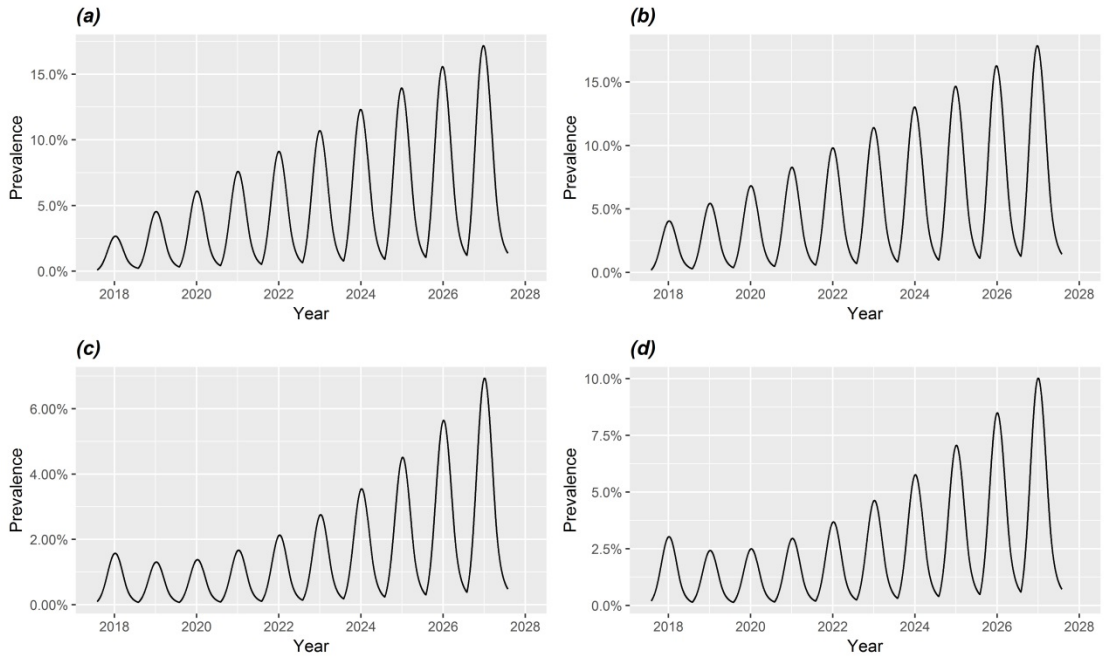

Figure 6-4 Predicted seasonal patterns of DD for 10 years with different initial lesion distributions. (a): one advanced lesion, (b): one advanced lesions & one early stage lesion, (c): one early stage lesion, (d): two early stage lesions

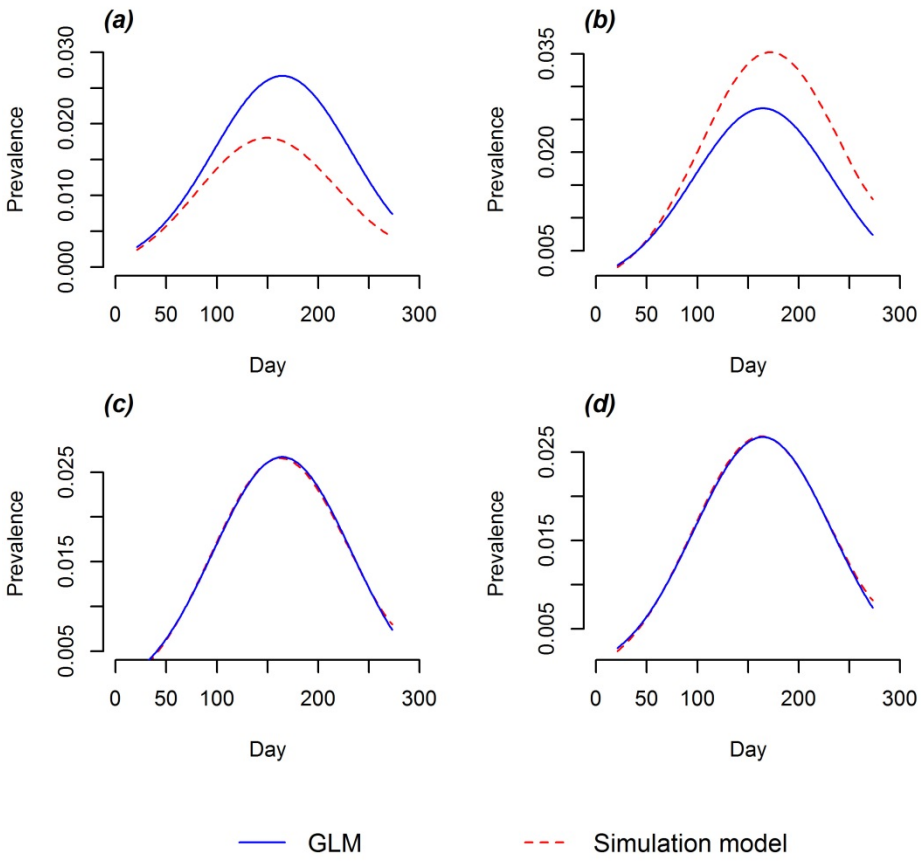

Figure 6-5 Results of sensitivity analysis with different values for α and θ. α: the reciprocal of the average time that early stage lesions persist, θ: probability that an early stage lesions progresses to an advanced lesion; (a): $\alpha = 0.0238$ animal/day and $\theta = 0.002$, (b): $\alpha = 0.0178$ animal/day and $\theta = 0.002$, (c): $\alpha = 0.0202$ animal/day and $\theta = 0.001$, (d): $\alpha = 0.0202$ animal/day and $\theta = 0.003$.

Table 6-1 Description of different stages of bovine digital dermatitis lesion using M scores.

M-score	Descriptor
M0	Normal skin.
M1	Early stage, small (<2 cm) focal active state. The surface is moist and ragged with mottled red-grey.
M2	Classical ulcerative active stage, usually large (>2 cm across). Painful upon palpation.
M3	Healing stage after antibiotic treatment. The ulcerated surface is covered by dry black scab.
M4	Chronic stage. The hyperkeratotic lesion can have a proliferative aspect.
M4.1	Chronic stage with small active M1 focus.

As described by Döpfer et al. (1997) and adapted by Berry et al. (2012)

Table 6-2 The parameters and their corresponding values used in the simulation model.

Parameter	Value	Descriptor
β_{t0}	0.0552	The transmission rate at the first day of lactation of every year in the model (1st August).
δ	0.00022	Deviation between the transmission rates of two consecutive days over a lactation season.
α	0.0202	Reciprocal of the time that an early stage lesion persists.
θ	0.002	Probability that an early stage lesion transits to an advanced lesion.

Table 6-3 Different scenarios tested in the sensitivity analysis for the simulation model.

Parameter	Sensitivity analysis scenarios			
	Scenario 1	Scenario 2	Scenario 3	Scenario 4
α	0.0238	0.0178	0.0202	0.0202
θ	0.002	0.002	0.001	0.003

α: Reciprocal of the time that an early stage lesion persists; θ: Probability that an early stage lesion transits to an advanced lesion

Additional files (See Appendix 5)

Additional file 1: Farm visits schedule. The table shows the schedule of the farm visits and frequencies of visits in each month from August 2017 to April 2018 in Waikato, New Zealand.

Additional file 2: Advanced bovine digital dermatitis lesions found in New Zealand. The three lesions were found by the first author in New Zealand dairy herds from 2015 to 2017.

Chapter 7. Inter-Observer Agreement between Two Observers for Bovine Digital Dermatitis Identification using the Digital Photographs in New Zealand

This chapter is prepared in the style format of New Zealand Veterinary Journal. The published manuscript is presented in appendix.

7.1. Abstract

7.1.1. AIMS

The aim of this study was to examine the inter-observer agreement for detecting bovine digital dermatitis (BDD) lesions in digital colour photographs of the hind feet of cows that had been taken while the animals were standing to be milked.

7.1.2. METHODS

Thirty-six photographs were selected from a total of 184 photographs held by the first author (R1). The selected photographs were then delivered to a technician (R2) who had previously visually inspected cattle for BDD lesions in Taranaki between 2014 and 2016. R2 recorded her judgement on the lesions shown in each photograph, and reported her results back to the R1. The feet were rated as being either BDD-positive or BDD-negative. No immediate prior training was given to R2 before she rated the photograph. The results from R2 were then compared with the R1's opinion on whether or not the photograph showed a cow with a BDD lesion. The percentage agreement and two other inter-observer agreement statistics i.e. Cohen's κ and Gwet's first-order chance correction agreement coefficient (AC1) were calculated and compared. The cumulative membership probabilities of the two agreement statistics were then calculated for each of the benchmark ranges.

7.1.3. RESULTS

The percentage agreement between R1 and R2 was 92% (33/36). Two inter-observer agreement statistics were calculated: Cohen' κ = 0.80 and AC1 = 0.86. The cumulative membership probability (75%) of AC1 fell in the benchmark range 0.81 to 1. This suggested we could be 75% sure that two observers had almost perfect

agreement. The cumulative membership probabilities for the range ≥ 0.61 were over 95% for both two agreement statistics suggesting we can be 95% sure the two observers at least had substantial agreement.

7.1.4. CONCLUSIONS

The two trained observers had at least substantial agreement in identifying from a digital photograph as to whether BDD lesions were present or absent. Therefore, results from the two could be used interchangeably.

7.1.5. CLINICAL RELEVANCE

Visual assessment for BDD lesions in the milking parlour can be subjective. However, a high agreement between these two trained BDD examiners means BDD prevalence reported from different regions in NZ by these two can be directly compared.

7.2. KEYWORDS

Dairy cattle, bovine digital dermatitis, visual assessment, inter-observer agreement, Gwet's AC1, probabilistic statement

7.3. List of abbreviations

AC1 – first-order chance correction agreement coefficient

BDD – bovine digital dermatitis

NZ – New Zealand

7.4. Introduction

Bovine digital dermatitis (BDD) is a dynamic infectious hoof disease which can cause lameness in dairy cattle. Since it was first identified, BDD has spread widely (Holzhauer *et al.* 2012; Solano *et al.* 2016; Yang *et al.* 2017a), particularly in countries where cattle are routinely housed for significant parts of the year (Palmer and O'Connell 2015). Traditionally, clinical inspection for BDD has been undertaken in a trimming crush or chute with the cow's feet lifted and carefully inspected. This inspection method has been adopted as a "gold standard" method by many researchers (Jacobs *et al.* 2017; Solano *et al.* 2017). However, it is time-consuming and heavily dependent on facilities. Lifting and inspecting cows' feet is particularly problematic in New Zealand (NZ) as most farms do not have dedicated foot crushes. Furthermore herd size is large with average 419 cows per herd (Anon 2017), while true cow level prevalence is low (Yang *et al.* 2017b), meaning that farmers are reluctant to spend the time necessary to properly identify BDD by lifting feet. One alternative to inspection of the lifted foot is inspecting cows' feet during milking (Thomsen *et al.* 2008). This is quicker than lifting feet, and only hind feet need examining because less than 3% of BDD affected cows have lesions on the front feet only (Laven and Proven 2000). If BDD is categorised into present/absent, parlour inspection during milking has a high specificity but moderate sensitivity (Thomsen *et al.* 2008; Yang *et al.* 2017b). However, as the inspection is subjective, different examiners could report different results even though they inspected the same population. It is thus essential to assess whether inter-observer agreement of BDD is generally high enough for BDD assessment results to be compared across studies.

Two methods have been used to assess inter-observer agreement for detecting BDD lesions: 1) clinical inspection of live animals (Holzhauer *et al.* 2006; Relun *et al.*

2011; Solano *et al.* 2017; Biemans *et al.* 2018) and 2) photographs (Manske *et al.* 2002; Armstrong *et al.* 2017; Solano *et al.* 2017). Holzhauer *et al.* (2006) reported fair to moderate agreement, i.e. four out of six scorers reported κ between 0.3 and 0.5 when BDD was categorised on a presence/absence scale. However, Relun *et al.* (2011) reported similar inter-observer agreement with κ 0.51 (95% CI=0.45–0.56), with a more complex BDD classification system – the M score which has been widely used to differentiate the morphological stages of BDD lesions (Döpfer *et al.* 1997; Berry *et al.* 2012). This may be because in contrast to Holzhauer *et al.* (2006) who had foot trimmers evaluating a range of lameness-causing disease the study by Relun *et al.* (2011) was focusing solely on BDD. Using the M score and observing cows in the milking parlour, Solano *et al.* (2017) reported higher inter-observer agreement with κ 0.74 (95% CI=0.69–0.78) than that reported by Relun *et al.* (2011). Solano *et al.* (2017) concluded that their higher level of agreement was due to continual training during the study period and the use of a reference card during scoring. Biemans *et al.* (2018) also reported similarly high inter-observer agreement using the M score in cattle in the milking parlour. Those authors assessed the inter-observer agreement immediately before they started data collection with κ 0.75 (95% CI=0.66–0.84) and twice during the data collection period with κ 0.85 (95% CI=0.78–0.93) and κ 0.76 (95% CI=0.61–0.90), respectively.

Three studies have used photographs to assess agreement. Manske *et al.* (2002) reported a moderate inter-observer agreement using a 5-point scale (κ = 0.46). Armstrong *et al.* (2017), using the M score reported a median percentage agreement with the modal score across 10 scorers of 63% (min 45%, max 75%). Using the same scoring system, Solano *et al.* (2017) evaluated inter-observer agreement twice during their study, and found that agreement midway through the study (κ 0.83 (95%

CI=0.74–0.9)) was marginally higher than agreement at the beginning (κ 0.77 (95% CI=0.67–0.86)).

Currently, no inter-observer agreement for detecting BDD lesions has been undertaken in NZ using either method. The difference in presentation between BDD in NZ and that in the northern hemisphere where previous validation studies have been undertaken (i.e. predominance of small grey lesions with a much lower percentage of ulcerative lesions; Yang *et al.* 2017a) means that NZ-specific data are needed. If it can be shown that there can be good inter-observer agreement between trained observers it simplifies the collection of data across the country from multiple observers.

Most studies of inter-observation agreement, have used benchmark ranges to interpret the agreement statistics (e.g. Landis and Koch (1977); Table 1). However, simply matching the calculated coefficient with the benchmark ranges can be misleading, as it ignores the certainty of the estimate of the agreement statistic; i.e. a coefficient value of 0.7 has more certainty if it is based on many subjects than the same value based on a small number of subjects. Therefore, a probabilistic statement may be useful, i.e. if the calculated κ is 0.7, what is the probability of κ falling within the range 0.61–0.8? This probability is defined as membership probability (Gwet 2014). However, in some circumstance, the probability of the agreement statistic falling within a specific range may be insufficiently high to meet our preferred level of certainty (e.g. 95%). In such cases, the cumulative membership probabilities for each of the benchmark ranges need to be computed (Gwet 2014).

We therefore conducted a validation study to assess inter-observer agreement in detecting BDD lesions in photographs taken of animals standing in the milking parlour, between the first author of this paper (R1) and a veterinary technician (R2)

who had previously been trained to inspect cattle for BDD lesions. Three agreement statistics, and, if relevant, their associated cumulative membership probabilities were calculated.

7.5. Materials and methods

7.5.1. Sample size determination and sample selection

It is important to notice the inter-observer agreement coefficient calculated from the sample is an estimate of the "true" agreement coefficient of the population. The estimated agreement coefficient is considered to be valid if it differs from its "true" value by less than an arbitrary relative error. According to above, sample size was determined using the following equation which was based on the variance formulas of κ-like coefficients (Gwet 2008): $n = m/(1+m/M)$, where $m = 1/r^2(p_a - p_e)^2$. In this equation, n is the required sample size; M is the total number of photographs held by R1 (184); p_a and p_e are percentage agreement and chance agreement respectively and r is the relative error. It can be seen from the equation that the sample size will be higher if the relative error is small. Similarly, given a smaller difference between the percentage and chance agreement, a larger sample size will be required. At this stage of the design, we had no idea of the value of $p_a - p_e$; we assumed it was 50% and set r as 30%. Therefore, a total of 36 photographs were selected by R1 who had examined 59,849 cows for BDD on 127 farms (Laven and Yang 2017) and delivered to R2 who had examined 60,455 cows for BDD on 224 farms (Yang *et al.* 2017a). R2 was required to identify the feet as BDD positive or negative. Out of these 36 photographs, 25 of them were considered to be BDD positive and 11 were considered as BDD negative by R1. Due to the shortage of BDD negative photographs, all of them (in total 11) were selected including normal feet (9

photographs) and feet with other problems such as foot rot (one photograph) and traumatic injury (one photograph). The 25 BDD positive photographs were the clearest (subject to R1's opinion) from the photograph pool to make sure the scoring conditions were as close as possible to detecting BDD in live animals. Being clear only meant those photographs were not taken at a bad angle or not blurred rather than whether they showed the largest or the most obvious lesions. These photographs had been taken from the same position in relation to the feet of the cows by digital camera in dairy herds in four different regions of NZ: Taranaki, Waikato, Manawatu and Canterbury. None of these photographs had been taken by R2, so she had no prior knowledge of them. Additionally, there was no discussion about the criteria for identifying BDD lesions before R2 rated the photographs. This allowed R2 to identify BDD lesions purely based on her previous experience in Taranaki, NZ (Yang *et al.* 2017a).

7.5.2. Statistical analysis

A standard 2X2 table was used to summarise the distribution of the results. Three measures of agreement were then calculated:

1) Percentage agreement, calculated as per Gwet (2008).

2) Cohen's κ (Cohen 1960).

3) Gwet's first-order chance correction agreement coefficient (AC1) (Gwet 2008), a more stable agreement coefficient to overcome the paradoxes related to κ (Feinstein and Cicchetti 1990). This agreement measurement calculates the chance agreement differently from Cohen's κ. Calibration for chance agreement of AC1 makes it consistent with the tendency of random ratings suggested by the observed rating results.

For the latter two agreement statistics, the cumulative membership probabilities for each benchmark range were calculated using AgreeStat 2015 (Advanced Analytics, LLC, Gaithersburg, Maryland, USA).

7.6. Results

The numbers of cases identified as negative or positive for BDD by R1 and R2 are summarised in Table 2. The two photographs which were reported as positive by R2 but negative by R1 were a picture of a normal foot with black pigment and a picture of foot with a traumatic injury (Figure 1). The percentage agreement was 92% (33/36). The two inter-observer agreements were 0.80 (95% CI=0.57–1) for Cohen's κ and 0.86 (95% CI= 0.69–1) for AC1. The cumulative membership probabilities for each coefficient within each benchmark range are displayed in Table 3. The results suggested that no matter which agreement statistic was used, we could always be more than 95% sure that the two observers had a substantial agreement. If AC1 was used, we could be 75% sure that the two had almost perfect agreement.

7.7. Discussion

Overall, the agreement between the two observers was at least substantial, and for AC1 it was highly likely to be almost perfect. This was despite 1) R2 not having done BDD-related work for over two years; and 2) photographs being used rather than live animals, as, even with the best quality photographs, diagnosis of BDD is not as easy from a photograph as it is in a live animal in a milking parlour, where multiple views of the lesion can be made. Both of those issues would tend to reduce agreement. The data thus strongly suggest that when BDD is assessed on NZ dairy farms during milking on a presence/absence basis any differences in results between two trained

observers are unlikely to have an appreciable impact on estimated BDD prevalence. Though we suggest that regular training and assessment of agreement is likely to further minimise any risk of clinically significant disagreement.

Using 40 digital photographs, Solano *et al.* (2017) found similar inter-observer agreements with κ 0.77 (95% CI=0.67–0.86) at the start or the midway of the study with κ 0.83 (95% CI=0.74–0.90) using the 5-point M score. This level of agreement was similar to that seen in the present assessment with κ 0.80 (95% CI=0.57–1), even though we used a simple presence/absence scale. One potential reason for this is that R2 had stopped doing BDD-related work for over two years, highlighting the suggestion by Solano *et al.* (2017) that continual training is important for maximising inter-observer agreement. Another potential reason is the much smaller lesions seen in this study compared to those seen in Canada (where the study by Solano *et al.* 2017 was undertaken). Smaller lesions are more difficult to identify (Thomsen *et al.* 2008), and this may be particularly the case with photographs where only one view is available.

However, many studies have shown that κ is an unreliable measure of agreement, especially when the assumption of the test that all observed ratings may yield an agreement by chance is incorrect (Gwet 2008). In a presence/absence test with two observers, the assumption will be incorrect when the cells of the two-by-two table are not balanced; i.e. when the prevalence of the trait is not close to 50% and/or when the sensitivities of the two observers are markedly different. Gwet (2008) introduced AC1 which accounts for these differences and therefore is more consistent with the percentage agreement. Despite these advantages (especially in regard to accounting for very low prevalences which are common in cattle medicine; e.g. BDD in NZ, Yang *et al.* 2017a), this agreement statistic has not been commonly used in the

veterinary literature (Clark-Price *et al.* 2017; Czopowicz *et al.* 2017; Buczinski *et al.* 2018), and not at all in BDD research. We would strongly recommend the use of AC1 in future tests of inter-observer agreement.

In addition to calculating a more robust agreement coefficient, this paper also used a probabilistic interpretation of the agreement coefficients. This process overcomes the problem of interpreting the agreement based on the calculated coefficient alone when the 95% confidence interval covers more than one benchmark range. In contrast, the cumulative membership probability explicitly provides information about how certain we are that the agreement coefficient falls within a certain benchmark range. In this study there was 75% probability that the actual agreement between the two observers was almost perfect, based on the AC1.

Currently, only a few people have been involved in monitoring BDD prevalence in NZ. In the future, if we want to maintain awareness of BDD, the best approach will be to have multiple observers who can easily visit farms within their regions and thus provide on-going data with minimal costs. This approach requires structured and on-going training program and will require regular validation (including measurement of inter-observer agreement) to ensure that subjective error has minimum impact on our estimates of disease prevalence in different regions.

7.8. Acknowledgements

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7.9. References

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Table 7-1 Landis and Koch (1977)'s benchmark for interpreting the inter-observer agreement.

Benchmark range	Strength of agreement
0.81 to 1.0	Almost perfect agreement
0.61 to 0.8	Substantial agreement
0.41 to 0.6	Moderate agreement
0.21 to 0.4	Fair agreement
0.01 to 0.2	Slightly agreement
≤0	Poor agreement

Table 7-2 The frequency distribution of the two observers' (the technician [OB1] and the first author [OB2]) judgements that if the feet were BDD positive (+) or negative (-) shown on the photos.

	OB2+	OB2-	Total
OB1+	24	2	26
OB1-	1	9	10
Total	25	11	36

Table 7-3 Cumulative membership probabilities of Cohen' κ and Gwet's first-order chance correction agreement coefficient (AC1).

		Cumulative membership probability	
Benchmark	**Interpretation**	**Cohen's κ**	**AC1**
≥ 0.81	Almost perfect	47.66%	75.03%[a]
≥ 0.61	At least substantial	96.22%	99.92%[b]
≥ 0.41	At least moderate	99.98%	100%
≥ 0.21	At least fair	100%	100%
≥ 0.01	At least slightly	100%	100%
≤ 0	Poor	100%	100%

a: there is 75% probability that the two observers have almost perfect agreement.
b: there is 99.9% probability that the two observers have at least substantial agreement.

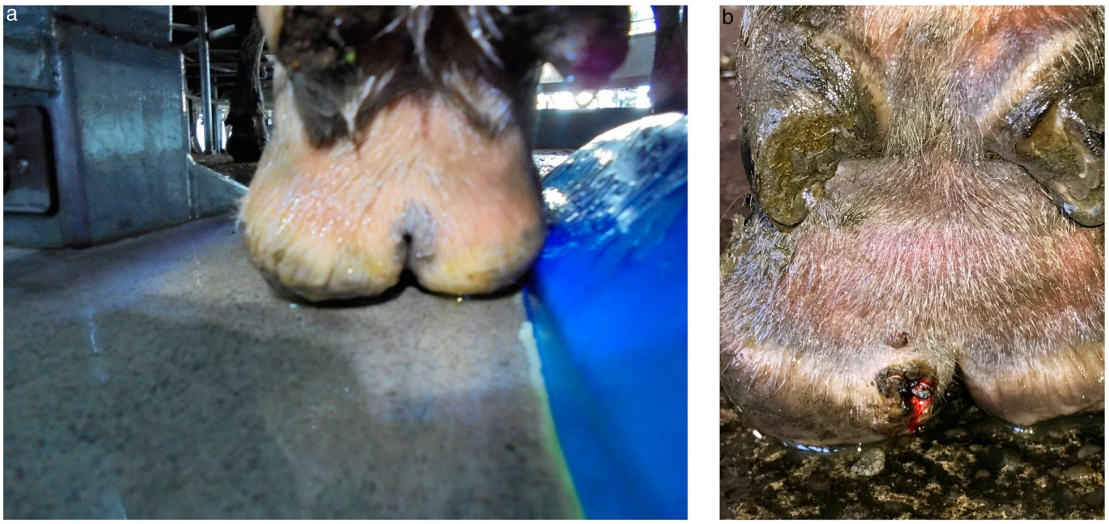

Figure 7-1 Photographs of (a) a normal cow's foot with black pigment and (b) a cow's foot with traumatic injury, which were identified by one observer (R2) as being positive for bovine digital dermatitis.

Chapter 8. Detecting bovine digital dermatitis in the milking parlour: To wash or not to wash, a Bayesian superpopulation approach

This chapter is prepared in the style format of The Veterinary Journal. The published manuscript is presented in appendix.

8.1. Abstract

Visual assessment in the milking parlour is a commonly used method to determine the prevalence and severity of bovine digital dermatitis (BDD). It is generally suggested that cows' feet are washed prior to examination to maximise the sensitivity of the assessment, but concern has been expressed that washing cows' feet could contaminate the teats and lead to intramammary infection. Furthermore, the evidence for washing cows' feet is equivocal, as some studies have reported similar sensitivities for detecting BDD without washing as that reported by studies which used washing. Furthermore most of these studies have used data from housed cattle. The findings from these studies may not be applicable to cattle at pasture where feet are often contaminated with mud rather than faeces and lesions may be smaller and less severe. The aim of this study was to compare, in cattle at pasture, the sensitivities of BDD examinations before and after washing.

Two herds known to have BDD were enrolled and approximately half of each herd was screened for BDD by examining the cows' hind feet before and after washing. The sensitivities of these examinations were estimated using a Bayesian superpopulation approach, and were found to be 0.34 (95% credible interval [CrI]: 0.088-0.69) and 0.63 (95%CrI: 0.46-0.78) for pre- and post-washing, respectively. There was a 93.95% probability that the sensitivity of examination post-washing was greater than that pre-washing. These results suggest that in pasture-based herds, many BDD lesions will be missed if cattle are examined without their feet being washed.

8.2. Keywords

Digital Dermatitis; Dairy Cattle; Pastoral; Diagnostic test evaluation; Bayesian latent class model

8.3. Introduction

Bovine digital dermatitis (BDD) is probably the most common infectious foot disease of dairy cattle. It has been reported in dairy herds in many countries under many different management systems, including the UK (Laven and Lawrence, 2006), the Netherlands (Holzhauer et al., 2012), France (Relun et al., 2013a), New Zealand (Yang et al., 2018) and Canada (Solano et al., 2016). BDD has a negative economic impact via its effect on milk production (Relun et al., 2013b) and through the cost of treatment (Cha et al., 2010). In addition to those losses, BDD is a painful condition which markedly reduces cow welfare (Bruijnis et al., 2012)

The examination of lifted feet has been widely considered as the reference method for detecting BDD lesions in cattle (Cramer et al., 2018; Solano et al., 2017). However, this requires restraint in a crush or chute and is thus a time-consuming method which makes routine screening for BDD unfeasible, particularly in countries such as New Zealand where both herd size and the ratio of cows to stockpeople are high. Routine screening for BDD is an essential part of BDD control and management (Döpfer et al., 2012), so alternatives to lifting feet are commonly used. Probably the most common alternative method used for BDD screening is examining cows' hind feet in the milking parlour during milking, with the usual recommendation being that cows' feet should be washed before they are inspected. This method has been reported to have an adequate sensitivity and a high specificity across different dairy systems when the outcome is a binary presence or absence of disease. For example, in Denmark, Thomsen et al. (2008) reported an overall sensitivity of 65% (95% confidence interval [CI]: 59%-72%) and a specificity of 84% (95%CI: 81%-87%), while in New Zealand, Yang et al. (2017a) reported that the sensitivity and specificity

were 63.1% (95% credible interval [CrI]: 45.1%-78.9%) and 99.9% (95%CrI: 99.8%-99.9%), respectively. In both of these studies feet were washed before examination.

However, in a study where cows' feet were not cleaned before examination, Cramer et al. (2018) reported a sensitivity and specificity that were similar to the values reported by Thomsen et al. (2008) and Yang et al. (2017a) (57.7% (95%CI: 53.2%-62.2%) and 95.3% (95%CI: 93.3%-96.8%), respectively). The data from Cramer et al. (2018) thus suggest that washing may not be necessary to achieve adequate sensitivity and a high specificity for detection of BDD.

Only one study has previously compared lesion detection pre- and post-washing: Oliveira et al. (2017) who evaluated the benefit of washing feet prior to screening for BDD in 22 housed dairy herds in Denmark. The herds were initially screened in the parlour in groups based on their order of entry into the milking parlour without washing of the feet. After each group was examined, their hind feet were washed and the group of cows was examined again. In order to minimise the risk of the observer remembering the first DD score, for the second observation every second cow in the row was scored followed by the remaining cows in row order. Oliveira et al. (2017) reported that apparent prevalence after washing was 1.32 times greater than the prevalence before washing. However as they did not record the details of the individual positive cattle, cattle identified as positive before washing could, potentially, be false positives which were negative after washing. If this was the case, this would mean that the true sensitivity of screening before washing was less than that reported by Oliveira et al. (2017). The aim of this study was to repeat the study undertaken by Oliveira et al. (2017) in pasture-based cattle, and in addition to identify and record every test positive cow, so that more information on the accuracy of

screening with and without washing could be collected, including estimates of sensitivities and specificities as well as the true prevalence of BDD in the two herds.

To estimate sensitivity and specificity without a "perfect" reference standard, the results of one or more diagnostic tests need to be collected and Bayesian methods can be used to estimate those parameters (Branscum et al., 2005). However, such analyses are often based on the binomial distribution, ignoring the fact that samples have been drawn from a finite population, whereas the binomial distribution requires an infinite population. If the sample size is much smaller than the population size the binomial distribution can still be used, but in situations where a high proportion of the population is sampled (typically >5%) the binomial method is no longer valid and an alternative such as hypergeometric sampling is required (Su et al., 2004). However, the hypergeometric distribution is a complex one, and analysis using such a distribution is often inflexible. This led to the development of the Bayesian superpopulation approach (Jones and Johnson, 2016) which postulates an infinite superpopulation(s) from which the actual finite population(s) has been drawn. This superpopulation approach allows the binomial method to be used even when the sample population is a high proportion of a finite population. The Bayesian superpopulation approach is thus a much simpler, and therefore more flexible, analysis than one based on the hypergeometric distribution.

The aim of this study was thus to compare, in pasture-based cows, the accuracy of BDD detection during milking before and after washing the feet using a Bayesian superpopulation approach.

8.4. Materials and methods

8.4.1. Study population

Two herds with 286 (herd 1) and 254 (herd 2) cows in the Waikato region of the North Island of New Zealand were selected. These two herds had been previously visited in January 2017 as part of a cross-sectional study of BDD prevalence across New Zealand (Yang et al., 2019) and been found to have BDD. In mid-January 2018, the first author visited the two herds to undertake the study. In each herd, only cows standing on one side of the herringbone parlour were examined in order to prevent any impact on milking time. On herd 1 and herd 2, 140/286 and 128/254 cows were examined, respectively.

In each herd, the hind feet of selected cows were initially visually examined for BDD without washing as soon as the cups were put on the teats. A cow was considered to be BDD positive if it had, on either hind foot, at least one erosive grey or black lesion or active red lesion at the back of the foot, (Yang et al., 2017b). If a cow was thought to have BDD, it was recorded in a notebook that the k^{th} cow in the m^{th} row was positive using the 'without washing method'. After all cows in a row had been examined, the notebook was folded and stored in a pocket to prevent the recorder reviewing the positions of positives cow before the post-washing examination. The cows' feet were then washed starting at the front of the row and moving backwards, after which the cleaned feet were examined. If a lesion was observed, it was recorded into a different notebook that the k^{th} cow on the m^{th} row was positive using the 'washing method'. The recorder was therefore not able to review the positions of positive cows based on the pre-washing examination during the post-washing examination. In addition, the recorder focused on examining BDD lesions rather than figuring out the position within the row of the cow the recorder was

examining. A cow's position within a row was only calculated after a cow was identified as positive. Thus cows which were identified as positive by the pre-washing examination were not examined more (or less) closely at the post-washing examination than those which had been identified as negative.

8.4.2. Statistical methods

As two diagnostic methods were used, four outcomes were possible: positive on both methods (++), positive with washing but negative without washing (+−), negative with washing but positive without washing (− +) and negative on both (−−). The counts for each scenario for the i^{th} herd could be written as $y_i = (y_{i1}, y_{i2}, y_{i3}, y_{i4})$. For the i^{th} herd, the number of sampled cows was $n_i = \sum_{j=1}^{4} y_{ij}$, where n_i was sampled from N_i, which is the herd size, in this case $N_1 = 286$ and $N_2 = 254$.

By combining the sensitivities and specificities of the two methods, the superpopulation model could be defined as:

$$y_i|\pi_i, \eta_1, \theta_1, \eta_2, \theta_2 \sim multinomial\ (n_i; p_{i1}, p_{i2}, p_{i3}, p_{i4})$$

where π_i is the true cow level prevalence of the i^{th} superpopulation; η_1, η_2 and θ_1, θ_2 are the sensitivities and specificities for detecting BDD with washing (method 1) and without washing (method 2), respectively; and $p_{i1}, p_{i2}, p_{i3}, p_{i4}$ are the observed proportion of $++, +-, -+, --$ respectively. The observed proportions based on the two correlated diagnostic methods (Oliveira et al., 2017) could then be formulated according to Georgiadis et al. (2003), where $T_1^{\pm}$, $T_2^{\pm}$ and $D^{\pm}$ were test positives/negatives by method 1, test positives/negatives by method 2 and the unknown true disease status (postive/negative), respectively:

$$p_{i1} = \boldsymbol{\pi_i} * P(T_1^+, T_2^+|D^+) + (1 - \pi_i) * P(T_1^+, T_2^+|D^-)$$

$$p_{i2} = \pi_i * P(T_1^+, T_2^-|D^+) + (1 - \pi_i) * P(T_1^+, T_2^-|D^-)$$

$$p_{i3} = \pi_i * P(T_1^-, T_2^+|D^+) + (1 - \pi_i) * P(T_1^-, T_2^+|D^-)$$

$$p_{i4} = \pi_i * P(T_1^-, T_2^-|D^+) + (1 - \pi_i) * P(T_1^-, T_2^-|D^-)$$

where:

$$P(T_1^+, T_2^+|D^+) = \boldsymbol{\eta_1} * \boldsymbol{P}(\boldsymbol{T_2^+}|\boldsymbol{T_1^+}, \boldsymbol{D^+})$$

$$P(T_1^+, T_2^-|D^+) = \eta_1 - P(T_1^+, T_2^+|D^+)$$

$$P(T_1^-, T_2^+|D^+) = (1 - \eta_1) * \boldsymbol{P}(\boldsymbol{T_2^+}|\boldsymbol{T_1^-}, \boldsymbol{D^+})$$

$$P(T_1^-, T_2^-|D^+) = 1 - P(T_1^+, T_2^+|D^+) - P(T_1^+, T_2^-|D^+) - P(T_1^-, T_2^+|D^+)$$

$$P(T_1^+, T_2^+|D^-) = 1 - P(T_1^+, T_2^-|D^-) - P(T_1^-, T_2^+|D^-) - P(T_1^-, T_2^-|D^-)$$

$$P(T_1^+, T_2^-|D^-) = (1 - \boldsymbol{\theta_1}) * \boldsymbol{P}(\boldsymbol{T_2^-}|\boldsymbol{T_1^+}, \boldsymbol{D^-})$$

$$P(T_1^-, T_2^+|D^-) = \theta_1 - P(T_1^-, T_2^-|D^-)$$

$$P(T_1^-, T_2^-|D^-) = \theta_1 * \boldsymbol{P}(\boldsymbol{T_2^-}|\boldsymbol{T_1^-}, \boldsymbol{D^-})$$

thus we then have:

$$\eta_2 = P(T_1^+, T_2^+|D^+) + P(T_1^-, T_2^+|D^+)$$

$$\theta_2 = P(T_1^-, T_2^-|D^-) + P(T_1^+, T_2^-|D^-)$$

note: $P(T_1^+, T_2^+|D^+)$ means the probability of both diagnostic methods returning a positive given the cow was truly BDD positive. The rest of the probabilities are then straightforward to interpret. The parameters in bold font in the equations required prior specification.

We then defined the conditional correlations between the outcomes of the two diagnostic methods:

$$\rho^+ = \frac{P(T_1^+, T_2^+|D^+) - \eta_1\eta_2}{\sqrt{\eta_1(1-\eta_1)\eta_2(1-\eta_2)}}$$

$$\rho^- = \frac{P(T_1^-, T_2^-|D^-) - \theta_1\theta_2}{\sqrt{\theta_1(1-\theta_1)\theta_2(1-\theta_2)}}$$

Analogous to the positive predictive value in one test in one population, the predictive value q_i for $++, +-, -+, --$ was then calculated:

$$q_i^{++} = \frac{\pi_i * P(T_1^+, T_2^+ | D^+)}{p_{i1}}$$

$$q_i^{+-} = \frac{\pi_i * P(T_1^+, T_2^- | D^+)}{p_{i2}}$$

$$q_i^{-+} = \frac{\pi_i * P(T_1^-, T_2^+ | D^+)}{p_{i3}}$$

$$q_i^{--} = \frac{\pi_i * P(T_1^-, T_2^- | D^+)}{p_{i4}}$$

The interpretation of these is straightforward, for example, q_i^{++} is the probability of a cow being truly BDD positive given that both methods returned a positive result. From this, the numbers of truly BDD positive cows within the four result groups (i.e. $++, +-, -+, --$) could be expressed as:

$$Y_i^{++} | y_i, \pi_i, \eta_1, \theta_1, \eta_2, \theta_2 \sim binomial\ (q_i^{++}, y_{i1})$$

$$Y_i^{+-} | y_i, \pi_i, \eta_1, \theta_1, \eta_2, \theta_2 \sim binomial\ (q_i^{+-}, y_{i2})$$

$$Y_i^{-+} | y_i, \pi_i, \eta_1, \theta_1, \eta_2, \theta_2 \sim binomial\ (q_i^{-+}, y_{i3})$$

$$Y_i^{--} | y_i, \pi_i, \eta_1, \theta_1, \eta_2, \theta_2 \sim binomial\ (q_i^{--}, y_{i4})$$

Similarly, for the unsampled portion of the herd, we have the number of truly BDD positive Y_i^U among those not sampled:

$$Y_i^U | y_i, \pi_i, \eta_1, \theta_1, \eta_2, \theta_2 \sim binomial(\pi_i, N_i - n_i)$$

So the total number of truly BDD positive $Y_i = Y_i^U + Y_i^{++} + Y_i^{+-} + Y_i^{-+} + Y_i^{--}$, for $i = 1, 2$. Finally, the true BDD prevalence λ_i of i^{th} herd was calculated as $\lambda_i = Y_i / N_i$.

The priors for the prevalence of BDD in the two superpopulations from which the two herds had been drawn were based on general data on the cow level prevalence

of BDD in New Zealand and, more specifically, from the previous examination of these two herds. Yang et al. (2017b) reported that in New Zealand, the apparent cow level prevalence in an affected herd was 1.7% (95%CI: 1.4%-2.1%) with the highest within-herd prevalence being 12.7%. The true cow level prevalence in an affected herd was estimated at 2.9% (95%CrI: 2.1%-4.3%) using a Bayesian latent class model (Yang et al., 2017a). The previous visits to the two herds in 2017 had found that herd 1 and herd 2 had had around 5% and 10% of cows, respectively, with visible BDD lesions that been detected by visual examination during milking. Since the sensitivity of detecting BDD visually in the milking parlour was reported as 63.1% in New Zealand (Yang et al., 2017a), these figures were likely to be an underestimate of the true prevalence. Furthermore, as BDD infection is dynamic within a herd (Capion et al., 2012), prevalence may vary between years; therefore the priors were based on combining data on the general BDD prevalence in New Zealand and the previous prevalence of BDD observed in these two herds. For superpopulation 1, our best estimate (mode) was that 4% of cows truly had BDD lesions and we were 95% sure that the true prevalence was less than 10%. This could be translated to beta (3.919, 71.0559). For superpopulation 2, our best estimate was 8% and we were 95% sure less than 15% of cows were affected, which was translated to beta (6.9835, 69.8101). Priors for the sensitivity (η_1) and specificity (θ_1) of method 1, respectively, have been widely published in different systems (Table 1). After considering the published values and the New Zealand situation, we adopted beta (20.9967, 11.7675) and beta (88.27996, 1.8816) for η_1 and θ_1, respectively. This indicated that our best estimate for η_1 was 0.65 and we were 95% sure it was greater than 0.5; and our best estimate for θ_1 was 0.99 and we were 95% sure it was more than 0.95. There was no prior

information available for$P(T_2^+|T_1^+, D^+)$, $P(T_2^+|T_1^-, D^+)$, $P(T_2^-|T_1^+, D^-)$ and $P(T_2^-|T_1^-, D^-)$, therefore a diffuse prior beta (1,1) was specified for them.

Because the model is not identifiable, using informative priors is a crucial part of the estimation of model parameters (Georgiadis et al., 2003). Hence, the resulting posterior inferences of the parameters could be dependent on these priors (Branscum et al., 2005). To assess to what extent posterior distributions depended on priors or data, a sensitivity analysis was conducted by changing the priors of the sensitivity and specificity of the washing method and the true prevalences in the two superpopulations. Nevertheless, the posteriors from the reasonable priors are our conclusions based on the data and our understanding of BDD in New Zealand, and should be considered as the final inferences from our model.

For the sensitivity analysis, optimistic (beta (9.6284, 3.8761)) and pessimistic (beta (150.1976, 123.0708)) priors for sensitivity of detection of BDD lesions were adopted. Being "optimistic" or "pessimistic" only referred to the mode of the prior distribution, it had no implications for our certainty in regard to the prior distributions. The optimistic prior indicated the mode was 0.75 and the 5th percentile 0.5, pessimistic prior indicated a mode of 0.55 and a 5th percentile was 0.5. A pessimistic prior beta (5.3842, 1.4871) was used for the specificity. This indicated a mode of 0.9 and a 5th percentile of 0.5. For the prevalence priors, we increased the estimates. For superpopulation 1, beta (2.0946, 10.851) was used, which indicated the mode was 10% and the 95th percentile was 35%. For superpopulation 2, beta (2.6371, 7.5485) was used, which indicated the mode was 20% and the 95th percentile is 50%.

The model was developed in OpenBUGS (Spiegelhalter et al., 2007). One chain ran for 50,000 iterations, after discarding 1000 iterations in the burn-in period. Model convergence was assessed using the time series plots.

8.5. Results

The raw test results of the two herds are summarised in a Table 2. The true cow level prevalence in herd 1 was estimated as 3.1% (95%CrI: 0.7%-6.6%) while the equivalent estimate for herd 2 was 6.3% (95%CrI: 2.8%-11.4%). The posteriors of the sensitivities and specificities of visual assessments with washing and without washing are shown in Table 3. Compared to visual assessment without washing, there was 93.95% probability that visual assessment with washing had a higher sensitivity, with the median difference in sensitivities ($\eta_1 - \eta_2$) being 0.29, the 6.5th percentile being 0.005 and the 93.5th percentile being 0.521 (87%CrI: 0.005-0.521). Figure 1 compares $\eta_1 - \eta_2$ based on the posterior to the same figure based on the prior. The difference in the specificities of the two diagnostic methods was not biologically important.

The sensitivity analyses showed that, the posterior prevalences of both finite herds were not sensitive to the priors of the cow level prevalences in the superpopulations or to the priors for the sensitivity and specificity of visual assessment with washing. Irrespective of the prior used, the estimates of the median prevalence were always around 3% and 6%. The sensitivity analysis also showed that there were clear differences between the prior and posterior distributions for the prevalences of BDD in both superpopulations (Figure 2), indicating that the posteriors for BDD prevalence were driven by the data not the priors.

Similarly, changing the prior for the specificity of visual assessment with washing had little impact on the posterior specificities of detection with or without washing. This is illustrated in Figure 3. Irrespective of which prior was used, the changes in the posterior medians of the specificities were < 0.01, for both methods. The prior of the sensitivity of visual assessment with washing influenced its posterior, i.e. increasing the prior mode by 0.1 resulted in an increase in the posterior median

of~0.06; decreasing the prior mode by 0.1 resulted in the posterior median decreasing by ~0.08. This is illustrated in Figure 4.

However, the posterior of the sensitivity of visual assessment *without* washing was not sensitive to the prior of the sensitivity of visual assessment *with* washing. Irrespective of the change in the prior of the sensitivity of visual assessment with washing, the posterior medians for the sensitivity of detection without washing remained at 0.34. The posterior medians and 95% credible intervals of the prevalences, sensitivities and specificities under different priors are summarised in Table 4.

8.6. Discussion

The traditional binomial method assumes the population size is infinite. While this is clearly an unjustified assumption in reality, assuming a binomial distribution can produce an acceptable approximated probability equivalent to that calculated using the hypergeometric distribution, when the sample size is < 5% of the herd size (Jordan and McEwen, 1998). However, in this study, the proportion of the herd that was sampled was ~50%. Therefore, the traditional Bayesian latent class model using binomial distribution could not be used with this data. This model therefore used the parameterisation developed by Georgiadis et al. (2003) to extend the Hui and Walter (1980) model using the Bayesian superpopulation approach as per Jones and Johnson (2016). Using this approach, the binomial method can be used to model this type of prevalence data providing a flexible and more straightforward alternative modelling method than the only other published alternative the hypergeometric method (Su et al., 2004).

On both farms, some cows were identified as BDD-positive before washing but negative afterwards (this was the case for 2 cows on herd 1 and 1 cow on herd 2).

Thus the positive results from the screening without washing were not just a subset of those from screening with washing method, as both methods identified unique positives. This confirmed the importance of identifying and recording positive cows rather than just recording overall prevalence.

The large difference 0.29 (87%CrI: 0.005-0.521) between the sensitivities of the two methods supports the hypothesis that screening BDD in the milking parlour without washing the hind feet prior to the inspection is very likely to miss BDD cases. In a herd with very low prevalence, as is common in New Zealand (Yang et al., 2017a, b), a positive herd could be reported as a false negative. Thus, screening without washing would not only underestimate cow level prevalence but also underestimate herd level prevalence.

In confined dairy systems where BDD prevalence is much higher (Solano et al., 2016), the sensitivity of visual assessment without washing appears to be higher than that reported in pasture-based systems (Cramer et al., 2018). This may be because high prevalence is also associated with lesions that are larger and more severe and thus more visible increasing the sensitivity of detection (Thomsen et al., 2008).

8.7. Conclusions

Visual screening for BDD without washing the feet prior to examination is not an appropriate method of BDD screening in pasture-based herds. Screening without washing is likely to result in underestimation of both herd and animal level prevalences. Using a binomial or multinomial Bayesian latent class models for hypergeometric data violates fundamental statistical assumptions. Although, practically, the posteriors for the sensitivities and specificities of diagnostic tests can be estimated by such models, it is worth using a more statistically correct and not

greatly more computationally difficult method to analyse the data. As such we would recommend that the superpopulation approach become the standard method for analyses such as the one described in this paper.

8.8. Conflict of interest statement

None to declare.

8.9. Acknowledgements

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Table 8-1 Estimates of sensitivity, specificity with 95% confidence intervals of visual inspecting bovine digital dermatitis lesions after washing cows' hind feet in milking parlour.

Source	Sensitivity	95%CI/CrI[a]	Specificity	95%CI/CrI
Rodriguez-Lainz et al. (1998)	72%	53%-86%	99%	93%-99%
Thomsen et al. (2008)[b]	65%	59%-72%	84%	81%-87%
Thomsen et al. (2008)[c]	84%	72%-97%	51%	42%-60%
Relun et al. (2011)[b]	90%	86%-94%	80%	75%-85%
Relun et al. (2011)[c]	94%	88%-99%	67%	48%-86%
Relun et al. (2011)[c]	79%	62%-96%	68%	59%-78%
Relun et al. (2011)[c]	91%	83%-99%	92%	87%-98%
Stokes et al. (2012)	100%		99%	
Yang et al. (2017a)	63.1%	45.1%-78.9%	99.9%	99.8%-99.9%

[a] 95%CI/CrI, 95% confidence interval or credible interval.
[b] Overall sensitivity and specificity across herds
[c] Sensitivity and specificity for herringbone herd

Table 8-2 Cross-classified test results for the visual assessment with feet washed and not washed.

Feet not washed before visual assessment	**Feet washed before visual assessment**	
	***T*+**	***T*-**
Herd 1		
***T*+**	1	2
***T*-**	2	135
Herd 2		
***T*+**	2	1
***T*-**	4	121

Table 8-3 Posterior distributions the sensitivities, specificities of visual assessments with feet washed and not washed prior to examination.

	Posterior median	95% Credible interval	
Sensitivity			
Feet washed	0.631	0.461	0.781
Not washed	0.34	0.088	0.688
Specificity			
Feet washed	0.989	0.97	0.998
Not washed	0.985	0.962	0.997

Table 8-4 Results of sensitivity analyses of the cow level prevalences within the two herds (λ_1 and λ_2), sensitivities (η) and specificities (θ) of visual assessments with feet washed (1) and not washed (2) prior to examination for bovine digital dermatitis of dairy cattle in New Zealand. The results were presented as posterior median (95% credible interval).

Parameter	**Sensitivity analysis scenarios**				
	Model[a]	Scenario 1[b]	Scenario 2[c]	Scenario 3[d]	Scenario 4[e]
λ_1(%)	3.1 (0.7, 6.6)	2.8 (0.7, 6.6)	3.5 (1, 7.3)	2.8 (0.7, 6.6)	3.5 (0.7, 8.4)
λ_2(%)	6.3 (2.8, 11.4)	5.9 (2.8, 11)	6.7 (2.8, 11.8)	5.9 (2.4, 11)	6.7 (2.4, 13.8)
η_1	0.631 (0.461, 0.781)	0.69 (0.432, 0.894)	0.548 (0.489, 0.607)	0.627 (0.458, 0.779)	0.62 (0.443, 0.777)
θ_1	0.989 (0.97, 0.998)	0.99 (0.97, 0.999)	0.989 (0.969, 0.998)	0.985 (0.959, 0.998)	0.989 (0.969, 0.999)
η_2	0.34 (0.088, 0.688)	0.35 (0.09, 0.692)	0.322 (0.081, 0.682)	0.346 (0.084, 0.715)	0.329 (0.086, 0.684)
θ_2	0.985 (0.962, 0.997)	0.985 (0.962, 0.997)	0.985 (0.963, 0.997)	0.983 (0.959, 0.997)	0.985 (0.963, 0.997)

[a] priors of the main model
[b] optimistic prior for sensitivity of visual assessment with washing
[c] pessimistic prior for sensitivity of visual assessment with washing
[d] pessimistic prior for specificity of visual assessment with washing
[e] increased estimates of prior for the prevalences of both herds

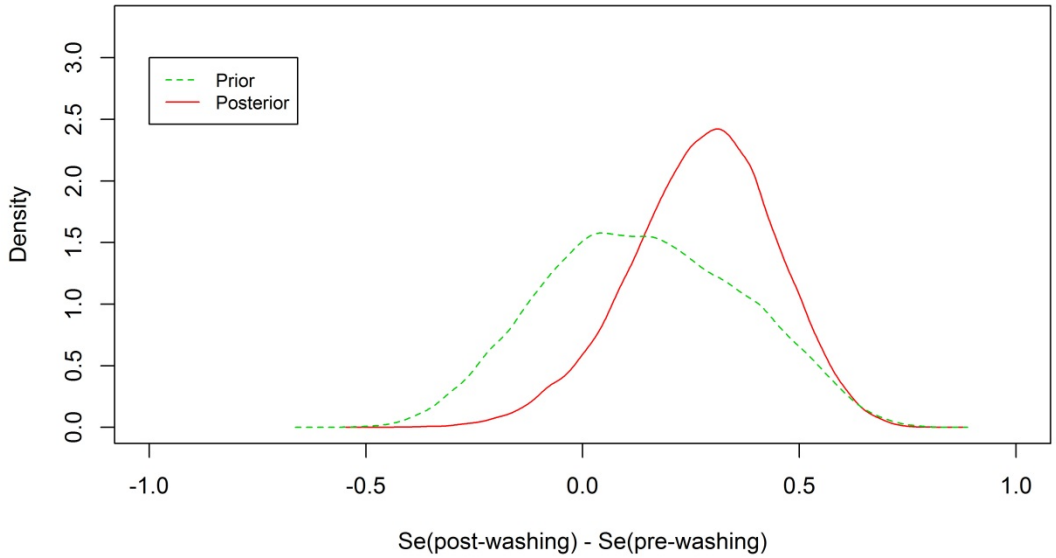

Figure 8-1 Contrast prior to posterior for difference in sensitivities (Se) of post-washing and pre-washing examinations.

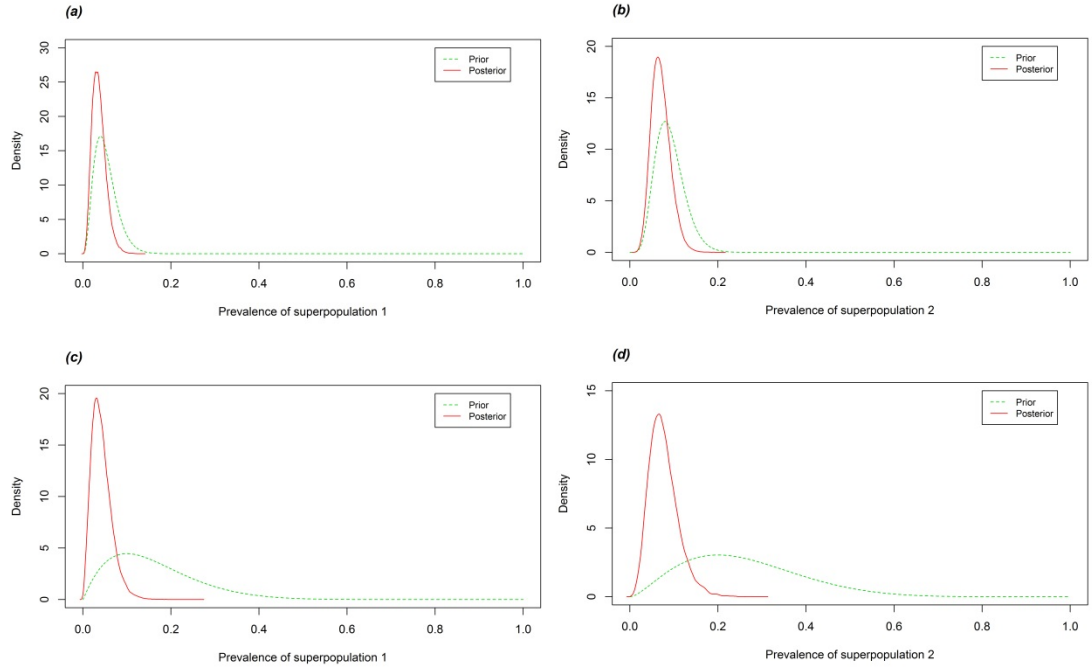

Figure 8-2 Contrast priors to posteriors for prevalence of bovine digital dermatitis in two superpopulations. Subplots (a) and (b) are based on the main model priors which are beta (3.919, 71.0559) and beta (6.9835, 69.8101); subplots (c) and (d) are based on the priors in sensitivity analysis which are beta (2.0946, 10.851) and beta (2.6371, 7.5485).

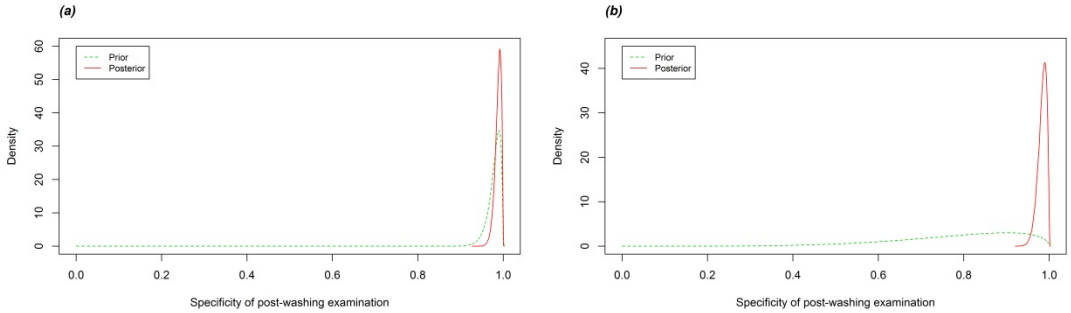

Figure 8-3 Contrast priors to posteriors for the specificity of post-washing examination for bovine digital dermatitis. Subplot (a) is based on the main model prior which is beta (88.27996, 1.8816); subplot (b) is based on the pessimistic prior used in the sensitivity analysis which is beta (5.3842, 1.4871).

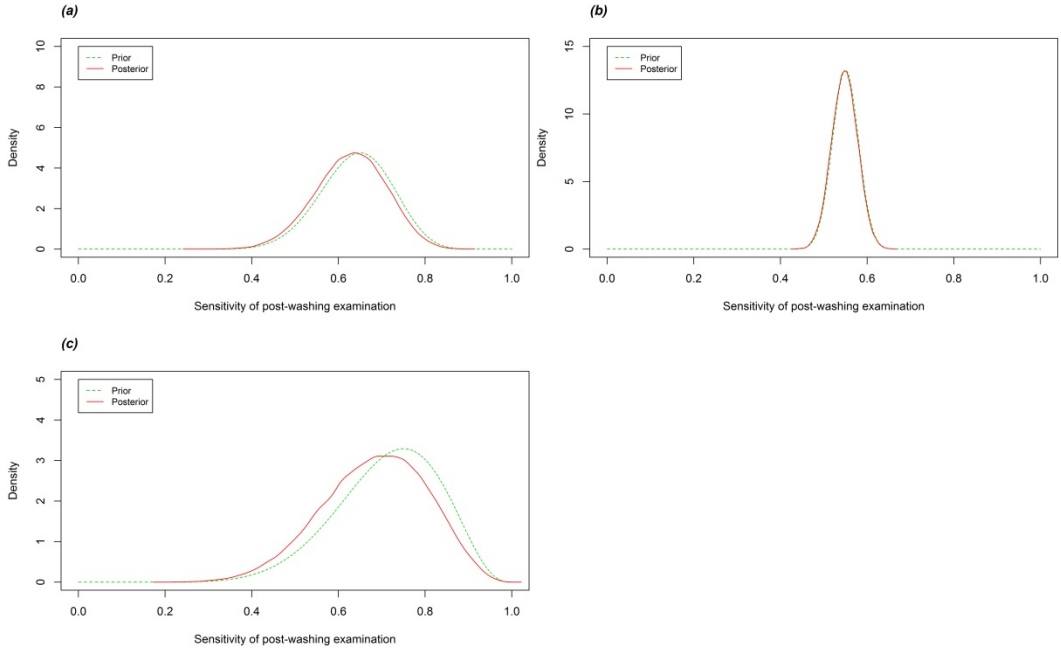

Figure 8-4 Contrast priors to posteriors for the sensitivity of post-washing examination for bovine digital dermatitis. Subplot (a) is based on the main model prior which is beta (20.9967, 11.7675); subplot (b) is based on the pessimistic prior used in the sensitivity analysis which is beta (150.1976, 123.0708) and subplot (c) is based on the optimistic prior used in the sensitivity analysis which is beta (9.6284,3.8761).

Chapter 9. General discussion

9.1. Overview

Bovine digital dermatitis (BDD) is an emerging disease in New Zealand, and prior to the studies presented in this thesis available information on BDD was limited to anecdotal and individual case reports. This thesis focused on providing basic epidemiological information of BDD in pasture-based dairy herds in New Zealand. The thesis addressed several issues associated with conducting epidemiological studies into BDD on New Zealand dairy farms. These problems include an imperfect diagnostic method resulting in biased prevalence estimates, sampling large proportions of animals from finite herds leading to the violation of the statistical assumption of the commonly used binomial method, limited previous studies on risk factors associated with herd level BDD status anywhere in the world, misclassification errors of herd level BDD status, limitations in our understanding of the importance of inter-observer agreement when recording the presence/absence of BDD lesions, arguments as to whether washing cows' feet was essential prior to visual examination, and understanding of transitions and persistence of BDD lesions inn New Zealand where the most commonly used M scoring systems/modelling framework may not be applicable. For each of these topics, the thesis provided solutions or answers in New Zealand dairy herds.

9.2. Prevalence

To overcome the misclassification errors and violation of the assumption of binomial distribution, we applied the Bayesian superpopulation approach that allows the use of a modified binomial method when inferences on finite herds. The study

was therefore able to robustly confirm that as well being present in Taranaki (Yang et al., 2017), BDD was also present in other regions of New Zealand. There were marked differences between regions in the herd and cow-level prevalence of BDD lesions with Manawatu having lower prevalence of disease at both levels than Waikato, South Canterbury, and Taranaki, with the West Coast having a high probability of being disease-free as of February 2017. This highlighted both the regions at higher risk of BDD and the wide presence of BDD across New Zealand which strongly indicates the disease is very likely to be present in untested regions of New Zealand such as Southland and Northland.

9.3. Farm management practices and climate effect

At the herd level, after adjusting for misclassification errors, animal movement, including purchasing heifers from other dairy herds and co-grazing heifers with animals from other properties, was associated with the increased probability that a herd having BDD lesions. At the cow level, having outside staff treat lame cows was associated with increased within-herd prevalence. Climate was also associated with BDD: increased rainfall in the previous month was associated with decreased cow level prevalence, while a quadratic relationship between prevalence and soil temperature was detected with peak prevalence occurring when the soil temperature was approximately 18℃.

These results provide a practical guide for managing BDD on seasonally calving pasture-based farms. Firstly, the best time to screen BDD is probably mid-spring to early summer (late October to end of January in New Zealand), as the prevalence of BDD is likely to be at its peak during this period. Control should focus on: 1) strict disinfection, between cows, of all knives and equipment used for hoof

trimming (especially if outside staff are used); 2) in dry weather hosing cows' feet to remove attached mud/slurry may be protective as it mimics a heavy rainfall environment; 3) when soil temperature is around 18°C, the use of a regularly cleaned and well drained stand-off pad may be useful to minimise disease spread, especially when it is dry; 4) when purchasing heifers, visual inspection of the whole heifer management group (not just the heifers for purchase) is recommended. If any of the heifers have visible lesion(s), then the entire group should not be purchased; 5) if youngstock such as heifers have to graze-off the farm, they should be reared as a single biosecure management group.

9.4. Inter-observer agreement

Interpretation of inter-observer agreement based on a calculated point estimate of an agreement coefficient such as Cohen's κ is misleading. The point estimate has a confidence interval and focusing only on central estimate ignores the accuracy of that estimate. For example, one may be less certain about the agreement amongst observers if the calculated κ value is based on a small number of subjects, and more certain if more subjects are used. Therefore a probabilistic interpretation is a better reflection of the agreement between observers. We therefore calculated the cumulative membership probabilities as per Gwet (2014) to quantify the inter-observer agreement. Results suggested that we can be 95% sure the two tested observers at least had substantial agreement in identifying whether BDD lesions were present or absent from a digital photograph. Therefore, BDD prevalence reported from different regions in New Zealand by these two observers can be directly compared as the influence due to subjectivity of the visual assessment in New Zealand was minimal.

9.5. The importance of washing cows' feet

The analysis suggested that compared to visual assessment without washing, there was a 93.95% probability that visual assessment with washing had a higher sensitivity, with the median difference in sensitivities being 0.29. The sensitivity of the visual assessment without washing was only 0.34 (95% credible interval [CrI]: 0.088-0.69), highlighting the importance of washing cow's feet prior to examination for BDD lesions in New Zealand.

9.6. Transmission dynamics of BDD

The M-score classification scheme (Döpfer et al., 1997; Berry et al., 2012) did not seem suited to describing the morphological stages seen in BDD lesions in New Zealand dairy cows. We, therefore modelled the dynamic transmissions of BDD within a herd using an alternative scoring system and model structure based on "Iowa DD scoring system" (Krull et al., 2016). This model was calibrated and validated against field data.

The model predicted that on infected dairy herds in New Zealand the prevalence of cattle with BDD lesions would remain relatively low by international standards (<18%) even after 10 years of within-herd transmission. This is likely to be due to the resolution of most clinical cases during late lactation and the subsequently low prevalence of infectious cattle at the start of the next lactation. Nevertheless, the model suggests that disease prevalence is likely to consistently increase over each subsequent lactation period, making it possible for BDD to become more clinically significant for New Zealand dairy herds in the future. The model also suggested that cattle with larger proliferative lesions had a stronger influence on the establishment

and maintenance of BDD than cattle with early stage lesions highlighting the importance of targeting animals with proliferative lesions for intervention or culling. On-going monitoring of BDD is highly recommended to assess the long-term progression of the disease in affected dairy herds.

9.7. Highlights of the thesis

Little information was available for BDD in the pastoral dairy system before this thesis certainly providing valuable epidemiological understanding of BDD in New Zealand. Apart from the veterinary aspect, novelty of the methodological approach adds extra value in this thesis. Some obvious or traditional approaches were not blindly accepted even if these approaches had been widely used in similar research topics; instead, each of the methods was queried and comprehensively discussed, which inspired the use of the most appropriate method for each study conducted.

One example is the use of the Bayesian superpopulation approach in number of the chapters. A common misunderstanding goes that when the entire herd is sampled, the number of positive cows in a herd can be modelled as a realization of a binomial random variable. A binomial random variable is the sum of n independent and identically distributed (iid) Bernoulli trials. When sampling animals, sampling without replacement is the most commonly used approach, hence, the distribution of the $k+1^{th}$ animal's test outcome depends on that of the k^{th} animal. Therefore, the observed (binary) test outcome of these animals cannot be adequately modelled as realization of sample of iid random variables. Instead, sampling could be described by the hypergeometric distribution. The difficulty of implementing hypergeometric approach was discussed; therefore a superpopulation approach which is theoretically

correct was adopted to model the hypergeometric data but using a much simpler method – the modified binomial approach.

Apart from the use of the Bayesian superpopulation approach, the thesis also identified the disadvantage of using a single calculated agreement coefficient to interpret the inter-observer agreement. The calculated agreement coefficient is just a point estimate, where its precision can be described by its standard error. Though the confidence intervals were usually provided, they were not carefully considered in the interpretation. For example, based on the confidence interval, it is correct to state the inter-observer agreement is somewhere between "moderate agreement" and "almost perfect agreement", while the point estimate can only report that the inter-observer agreement falls in a certain level. This is not always desirable unless the standard error of the estimator is small, e.g. the confidence interval does not cover more than one agreement levels. In addition, if the calculated agreement coefficient is considered as a function of the underlying random variables of the rating data, it is then an estimator which is always exposed to sampling variation. Therefore, the interpretation of the agreement must be associated with a degree of certainty. Hence a probabilistic approach was adopted in the thesis.

9.8. Future perspectives

9.8.1. Microbiology

Although *Treponema* spp. are suggested as being the most important bacterial species associated with BDD, little work has been done on the bacteriology of BDD in New Zealand. Future work could focus on evaluating the role of treponemes in BDD in New Zealand, especially understanding the heterogeneity of BDD-associated *Treponema* spp. and could use techniques such as bacteriological culture, and PCR at

the individual or microbiome level. One key area for research would be the development of a New Zealand-specific serological test (ELISA) for BDD. This might help explain why the great majority of BDD affected cows in New Zealand are type I animals (no M2 lesions identified). As per Gomez et al. (2014), compared to animals with no BDD lesions observed, antibody titres in animals diagnosed with at least one M1 or M4.1 but no M2 lesions did not increase after lesion detection. If this is also true in New Zealand, lack of M2 lesions may be because of insufficient spirochetes or that the penetration of the microorganisms into the skin is not sufficiently deep enough to trigger an immune response.

Microbiological research could also help elucidate the process of BDD, as opposed to the current study which looked at development of BDD lesions. Microbiology could therefore enable the transmission dynamic of BDD in New Zealand dairy farms to be more accurately modelled and thereby increase the utility of modelling in the design of effective intervention and control methods for BDD on New Zealand dairy farms

9.8.2. Epidemiology

The epidemiological studies in this research program have concentrated on the disease distribution, risk factors and transmission dynamics of BDD. Although large number of farms and cows were involved in the research, it only covered five regions of New Zealand due to the intensive labour requirement and finite resources available. Nonetheless, the thesis provides information for future epidemiological investigation.

A larger-scale study could be conducted over a larger geographic area, aiming to provide accurate nation-wide figures. Data could be aggregated at the regional level and the analysis could be focused on an explanation of regional differences in disease

distribution which were not evaluated in this thesis. Appropriate sample sizes can be calculated based on parameters provided by our studies, although conducting a small scale pilot study in each of the region is highly recommended. Such a study could easily be combined with microbiological studies taking lesion biopsies and blood samples on sampled farms. These results would be useful to refine the statistical models, which could provide more accurate information to describe BDD infection and lesion status and better estimate the unbiased strength of association between covariates and animal level BDD status.

Our mathematical model based on the longitudinal observations identified the seasonality of BDD in New Zealand and predicted some future trends. However, the model did not have a compartment describing the latent infected class because infected animals without a clinical lesion cannot be observed. Combining longitudinal studies with microbiological research could result in more accurate modelling of the transmission/infection dynamic. In addition an individual level stochastic model could also be developed to investigate the dynamics and progression of the disease at animal level.

9.8.3. Prevention

Microbiological and epidemiological studies are essential to determine the aetiology, pathogenesis, distribution, frequency, associated factors and dynamics of BDD. However, although recommendations for preventative strategies could be derived from the studies in this thesis, the effectiveness of such strategies cannot be determined. Field intervention studies will thus be an essential component of the future research, because practical and effective prevention strategies are required to keep BDD prevalence as low as possible in New Zealand. Given that BDD is highly

contagious and eradication of the disease on affected farms has never been successful, the New Zealand situation might be useful for vaccine development. If animals without lesions (low antibody titre) are vaccinated and therefore acquire long-lasting immunity (optimally but not essentially life-long), then infection will be restricted to only a small number of animals. If these animals are identified and culled then we can eradicate disease from the farm and potentially the whole of the country.

9.9. References

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Appendix

Appendix 1: Published article: Farm level risk factors for bovine digital dermatitis in Taranaki, New Zealand: An analysis using a Bayesian hurdle model

Bovine Digital Dermatitis in cattle:
Confidential farm management questionnaire

2014

Please complete this questionnaire, fold and place in the envelope with the address showing, and post back to us.
All completed questionnaires will go in a draw each month for a package of lameness equipment including 2 new, sharpened hoof knives.

Peter Benn
Energy Vets Taranaki
524 Richmond Road
RD 3, New Plymouth 4373

For any queries, please contact 06 756 7228

About this questionnaire

This questionnaire is being undertaken under auspices of the BDD Working Group, which includes representatives from Massey University, the Ministry for Primary Industries, private veterinary practice (Energy Vets Taranaki) and DairyNZ (among others).

The aim is to increase our understanding of the disease under New Zealand conditions, including how much disease is currently being seen on dairy farms. This will enable us to identify trends in future.

This questionnaire should take 15-20 minutes to complete and your cooperation is much appreciated. It is being performed in conjunction with a herd screening for BDD. The aims are to describe husbandry and management practices that may be relevant to BDD. The questionnaire covers the following elements:

- general farm details and management;
- footcare procedures and BDD details specific to the farm;
- management procedures of different age groups of animals.

Background

Bovine Digital Dermatitis (BDD) is an infectious disease of the feet of cattle. It causes lesions which are mostly seen between the heel bulbs of the hind feet, especially in dairy cows. These lesions can be extremely painful and frequently cause lameness – hence the disease affects production as well as welfare.

In Europe and the US, when the disease is introduced into a herd, it tends to spread fast. A large percentage of the herd (20-40%) develops acute lesions that are characterised by skin loss, i.e. the surface of the lesion is lower than the skin. The lesions are reddish and poorly demarcated, bleed easily and are extremely painful to the touch.

Over time, the severity of the lesions tends to diminish, with most lesions becoming chronic. As a reaction to the infection, white fibres develop which give the lesion initially a stipply and later a 'warty' aspect. The lesions develop into nodules which are raised above the skin. These lesions tend to be less painful.

Acute erosive lesion (above); proliferative chronic lesion (left).

BDD in New Zealand

Cases suggestive of BDD have been observed in New Zealand for years. The disease was confirmed unequivocally in 2011. In 2012, the BDD Working Group was established to monitor the spread of disease, raise awareness and provide recommendations for prevention and control.

The early cases that were identified tended to be isolated and sporadic, and no outbreaks in the herd have been observed. However, there have been an increasing number of case reports, and there are indications that the prevalence (i.e. the percentage of animals affected) within the herds is increasing. The concern is that the disease may start spreading as it has done elsewhere in the world. The increasing use of indoor housing systems and feed pads, in combination with increasing stocking rates, use of supplementary concentrate feeding etc., are all factors which could at some point trigger epidemic outbreaks of BDD.

To date, we do not have a strong scientific understanding of the disease. Our objectives are to

- provide scientifically-based evidence to assess whether the disease is spreading or becoming more common;
- characterise the cases identified in New Zealand, and describe the patterns of disease within herds;
- develop relevant protocols and recommendations for identifying and controlling the disease.

Confidentiality

All information given will be treated with confidentiality. The farm details recorded on this page will be accessible to the principal researchers only. We will not contact you without your consent, and even if given, will not contact you unless necessary.

Farm details

1. Please complete the following contact details:

Name and farm address	_____ _____ _____ _____ _____
Email address	_____
Farm telephone / mobile	Tel. _____ Mobile_____
NAIT number	_____
FarmsOnLine number (if applicable)	_____
Person completing the questionnaire	☐ farm owner(s) ☐ farm manager(s) ☐ stockperson(s) ☐ other: _____
Date of completion	____ / ____ / 2014
Veterinary practice	_____

2. If you own or work on other farm(s), please complete the following. Otherwise, go to question 4.

Farm address (2) _____
_____
_____
_____
_____

NAIT number _____

FarmsOnLine number (if applicable) _____

Farm address (3) _____
_____
_____
_____
_____

NAIT number _____

FarmsOnLine number (if applicable) _____

3. Is there any movement between or exchange of stock (cows, heifers, calves or holdovers) between the farms you work on?

- ☐ yes
- ☐ no

Farm level variables

4. We would like to know the ***numbers of animals*** on the farm at this moment. Please could you specify the approximate total numbers of the following categories of cattle:

Species / type	**Total number on farm on date of screening**
Calves / heifers	
Dairy cows (i.e. milking or dry)	
Fattening cattle	
Breeding bulls	
Beef cattle	
Grazing heifers	
Other	

5. Bringing animals onto the farm from outside is one of the most important ways of introducing BDD on previously negative farms. How many of the following animals have been brought onto the farm ***in the last 12 months***?

Category / group	**Number of animals**	**Source(s) of acquired animals (tick all that apply)**
Calves / heifers		☐ other farmer ☐ market ☐ known dealer
Dairy cows (i.e. milking or dry)		☐ other farmer ☐ market ☐ known dealer
Fattening cattle		☐ other farmer ☐ market ☐ known dealer
Breeding bulls		☐ other farmer ☐ market ☐ known dealer
Grazing heifers		☐ other farmer ☐ market ☐ known dealer
Any other cattle (specify)		☐ other farmer ☐ market ☐ known dealer

6. Calving season: what is the average percentage of calves born in:

- ☐ autumn _____ %
- ☐ spring _____ %
- ☐ winter _____ %
- ☐ summer _____ %

7. ***Young stock grazing***. If you use a runoff or grazier at an address that is separate from your main farm(s), please complete the following. Otherwise, go to question 8.

Address of grazing farm _____

_____

_____

_____

_____

NAIT number _____

FarmsOnLine number (if applicable) _____

8. If you provide grazing for stock from another farm, please complete the following. Otherwise, go to question 9.

Address of origin of stock	_____ _____ _____ _____ _____
NAIT number	_____
FarmsOnLine number (if applicable)	_____

If relevant, please provide further details for stock grazed off the farm or brought onto the farm for grazing, e.g. how many, for how long etc.

Stock grazed off this holding	Stock brought onto this holding for grazing

9. ***Animal transport***. Which of the following apply?

- ☐ I transport animals in my own truck
- ☐ I walk animals to grazing only
- ☐ I use a transport company, namely: _____

10. Do you share trucking or a loading ramp e.g. with your neighbour(s)?

- ☐ yes
- ☐ no

Bovine digital dermatitis on the farm level

11. Do you believe you have ***ever*** seen BDD on your farm?

- ☐ yes
- ☐ no (go to 15.)

12. If you think you've seen it, in which ***year*** did you first notice it? _____

13. Since the first time you saw it, which of the following statements best describe BDD cases (provide more info in the box):

- ☐ saw only one case, never again
- ☐ the odd case, periodically
- ☐ a gradually increasing number of cases per year

14. Have you noticed a specific ***seasonal or time of year*** in the occurrence of BDD?

- ☐ no, any time of year
- ☐ yes, I tend to see the cases in _____

Hoof care

15. Which of the following best describes the farm strategy regarding hoof trimming?

- ◻ routine (preventative or functional) trimming, on regular basis
- ◻ lame cows only (curative trimming), when necessary
- ◻ not performed
- ◻ other:

16. ***Who*** trims the hooves of cattle on the farm? (tick all that apply)

- ◻ farmer _____ % of total; formally trained? yes / no
- ◻ stockman / stockmen _____ % of total; formally trained? yes / no
- ◻ certified hoof trimmer _____ % of total
- ◻ vet _____ % of total
- ◻ other: specify _____ _____ % of total

Farm management

17. **Housing system(s) used**. Tick as many of the following as apply currently; you may use the text box to provide specific information.

	Lactating cows	**Dry cows**
Housing system(s) used	◻ pasture ◻ indoor / cubicles ◻ straw yards ◻ feed pads ◻ straw yards	◻ pasture ◻ indoor / cubicles ◻ straw yards ◻ feed pads ◻ straw yards
Frequency of cleaning out bedding	☐ after each group ☐ never: dissipates spontaneously ☐ other: specify _____	☐ after each group ☐ never: dissipates spontaneously ☐ other: specify _____

18. Have there been any major management changes in the previous 5 years, that have not been captured in the questions above but which you believe could have an influence on BDD? If so, could you describe these? (e.g. investment in new milking shed, construction of feed pads, modifications of housing for young stock or cows, substantial changes in nutrition etc.)

_____

_____

_____

_____

_____

19. Are there any other pieces of information you believe may be relevant to BDD on this farm, or elsewhere?

_____

_____

_____

_____

_____

Negative Binomial Hurdle Model with Covariates in Bayesian Paradigm

The negative binomial (NB) hurdle model is a two stage modelling process. The first part is a binary model that measures whether or not the farms had zero cases. The second part is a zero-truncated negative binomial model to describe the counts of cases in positive farms. Let Y_i denote the response such as BDD counts on ith farm. We then have such a probability distribution:

$$P(Y_i = y_i|p_i) = 1 - p_i, if\ y_i = 0$$

$$P(Y_i = y_i|\pi_i, r, p_i) = p_i \binom{y_i + r - 1}{y_i} \frac{{\pi_i}^r (1-\pi_i)^{y_i}}{1 - {\pi_i}^r}\ , if\ y_i > 0$$

When adding covariates in, such as to evaluate the associations between the predictors and the outcome, a simultaneous inference would be made about if the farm had non-zero cases and count process conditional the farm had ≥1 case. Usually, covariates related to p_i and the NB mean λ_i can be modelled using logit model and log-linear model.

$$\lambda_i = \frac{r(1-\pi_i)}{\pi_i} = \mu_i n_i$$

$$\text{logit}(p_i) = \gamma X_i$$

$$\log(\lambda_i) = \log(n_i) + \beta X_i$$

where μ_i is the *rate per cow* and n_i is cows inspected in a farm which is the exposure term. X_i is the predictor vector and $\gamma = (\gamma_0, \gamma_1, \dots, \gamma_m)^T$ and $\beta = (\beta_0, \beta_1, \dots, \beta_m)^T$ are regression coefficient vectors. Define $\theta = \log(\text{r})$.

The likelihood function:

$$f(Y|\gamma, \beta, \theta)$$

$$= \prod_{i=0}^{k} \left(1 - \frac{e^{\gamma X_i}}{1 + e^{\gamma X_i}}\right) \prod_{i=k+1}^{j} \left(\frac{e^{\gamma X_i}}{1 + e^{\gamma X_i}}\right) \binom{y_i + e^{\theta} - 1}{y_i} \frac{(\frac{e^{\theta}}{e^{\theta} + e^{\beta X_i} n_i})^{e^{\theta}} (1 - \frac{e^{\theta}}{e^{\theta} + e^{\beta X_i} n_i})^{y_i}}{1 - (\frac{e^{\theta}}{e^{\theta} + e^{\beta X_i} n_i})^{e^{\theta}}}$$

where j is the total number of farm while a subset of k farms have zero values.

With covariates added, the priors are assigned on the regression coefficients and r. Without prior knowledge, we assigned independent normally distributed prior with mean ν and variance σ^2 each for γ, β and θ. The joint prior distribution:

$$f(\gamma,\beta,\theta) = \left(\frac{1}{\sqrt{2\pi\sigma_\theta}} e^{\frac{-(\theta-\nu_\theta)}{2\sigma_\theta^2}}\right) \prod_{i=0}^{m} \left(\frac{1}{\sqrt{2\pi\sigma_{\gamma i}}} e^{\frac{-(\gamma_i-\nu_{\gamma i})}{2\sigma_{\gamma i}^2}}\right) \prod_{i=0}^{m} \left(\frac{1}{\sqrt{2\pi\sigma_{\beta i}}} e^{\frac{-(\beta_i-\nu_{\beta i})}{2\sigma_{\beta i}^2}}\right)$$

We then applied Bayes' rule to get a joint posterior distribution with a nonstandard density:

$$f(\gamma,\beta,\theta|Y) \propto f(Y|\gamma,\beta,\theta) * f(\gamma,\beta,\theta)$$

$$\propto \prod_{i=0}^{k} \left(1 - \frac{e^{\gamma X_i}}{1+e^{\gamma X_i}}\right) \prod_{i=k+1}^{j} \left(\frac{e^{\gamma X_i}}{1+e^{\gamma X_i}}\right) \binom{y_i + e^\theta - 1}{y_i} \frac{(\frac{e^\theta}{e^\theta + e^{\beta X_i} n_i})^{e^\theta} (1 - \frac{e^\theta}{e^\theta + e^{\beta X_i} n_i})^{y_i}}{1 - (\frac{e^\theta}{e^\theta + e^{\beta X_i} n_i})^{e^\theta}}$$

$$* e^{\frac{-(\theta-\nu_\theta)}{2\sigma_\theta^2}} \prod_{i=0}^{m} \left(e^{\frac{-(\gamma_i-\nu_{\gamma i})}{2\sigma_{\gamma i}^2}}\right) \prod_{i=0}^{m} \left(e^{\frac{-(\beta_i-\nu_{\beta i})}{2\sigma_{\beta i}^2}}\right)$$

The posterior distribution is difficult to analyse mathematically, Markov Chain Monte Carlo (MCMC) technique, particularly, Gibbs sampling was used to obtain posterior estimations.

OpenBUGS Code of a Negative Binomial Hurdle Model

```
model {

  K<-10000

 for (i in 1:114) {

logit(p[i])<-
b[1]*sdairy[i]+b[2]*graze[i]+b[3]*shed[i]+b[4]*hfvet[i]+b[5]*season[i]+b[6]

log(lambda[i])<-
a[1]*sdairy[i]+a[2]*graze[i]+a[3]*shed[i]+a[4]*hfvet[i]+a[5]*season[i]+a[6]

mu[i]<-lambda[i]*hs[i]

psi[i]<-r/(r+mu[i])

z[i]<-step(y[i]-1)
                                        # I(Y>0)

ll[i]<-(1-z[i])*log(1-p[i]) + z[i]*(log(p[i])+loggam(y[i]+r)-loggam(r)-loggam(y[i]+1)
+ r*log(psi[i])+y[i]*log(1-psi[i]) - log(1-pow(psi[i],r)) )

zeros[i]<-0

zeros[i]~dpois(phi[i])

phi[i]<-  - ll[i]+K

}


for (j in 1:6) {

a[j]~dnorm(0,0.1)

b[j]~dnorm(0,0.1)

}

r<-exp(logr)

logr~dnorm(0,0.1)

alpha<-1/r

}
```

Appendix 2: Published article: Effects of climate and farm management practices on bovine digital dermatitis in spring-calving pasture-based dairy farms in Taranaki, New Zealand

Bovine Digital Dermatitis in cattle:
Confidential farm management questionnaire

2015-6

Confidentiality

All information given will be treated with confidentiality. The farm details recorded on this questionnaire will be accessible to the principal researchers only. We will not contact you without your consent, and even if consent is given, will not contact you unless necessary.

This questionnaire may be posted to Neil Chesterton

Neil Chesterton
Energy Vets Taranaki
18 Dudley Road Lower
RD 6, Inglewood, 4386

For any queries, please contact 06 756 7228

Farm details

1. Please complete the following contact details:

Name and farm address	_____ _____ _____
Email address	_____
Farm telephone / mobile	Tel. _____ Mobile_____
NAIT number	_____
FarmsOnLine number (if applicable)	_____
Person completing the questionnaire	☐ farm owner(s) ☐ farm manager(s) ☐ sharemilker(s) ☐ other: _____
Date of completion	____ / ____ / 201_
Veterinary practice	_____

2. Do you own or work on other farm(s)?

- ☐ yes
- ☐ no

If so please complete the following. Otherwise, go to question 3.

Farm address (2)	_____ _____ _____
NAIT number	_____
FarmsOnLine number (if applicable)	_____

Farm address (3)	_____ _____ _____
NAIT number	_____
FarmsOnLine number (if applicable)	_____

Stock information

3a. Do you have cows milking on more than one farm?

- ☐ yes
- ☐ no

3b. Is there any movement of these milking cows between the farms you work on?

- ☐ yes
- ☐ no

4. How many ***animals*** are on the farm where we screened the cows in October/November?

Type	**Number on this farm on date of screening**
Dairy Calves	
Dairy Heifers	
Dairy Cows	
Dairy Breeding bulls	
Beef cattle	
Other	

5. How many of the following animals have been brought or bought onto this farm ***in the last 12 months***?

Category / group	**Number of animals**	**Source(s) of acquired animals (tick all that apply)**
Dairy Calves		☐ directly from other farm/s ☐ sale yards
Dairy Heifers		☐ directly from other farm/s ☐ sale yards
Dairy Cows		☐ directly from other farm/s ☐ sale yards
Dairy Breeding bulls		☐ directly from other farm/s ☐ sale yards
Beef cattle		☐ directly from other farm/s ☐ sale yards
Any other cattle (specify)		☐ directly from other farm/s ☐ sale yards

Young stock grazing.

6a. Do your calves go away grazing off your farm/s.

- ☐ yes
- ☐ no

6b. If " Yes" – do your calves graze with calves from another farm?

- ☐ yes
- ☐ no

Older stock grazing.

7a. Do your cows go away grazing in winter?

- ☐ yes
- ☐ no

7b. If "yes" do they mix with other cows from other farms?

- ☐ yes
- ☐ no

8. Do you provide grazing for stock from other farms at your farm or run-off?

- ☐ yes
- ☐ no

Animal transport.

9. Have you used a transport company to transport animals in the last 12 months?

- ☐ yes
- ☐ no

10. Do you share a loading ramp with another farm(s)?

- ☐ yes
- ☐ no

Hoof care

11. ***Who*** treats your lame cows on the farm? (tick all that apply)

- ☐ yourself /farm staff
- ☐ vet
- ☐ certified hoof trimmer
- ☐ other: specify _____

12a. Do you have a foot bath?

- ☐ yes
- ☐ no

12b. Did you use your foot bath in the last 12 months?

- ☐ yes
- ☐ no

Farm management

12. **Housing / Feeding**. Tick as many of the following as apply currently

- ☐ feed pads
- ☐ herd home
- ☐ stand-off pad – winter only
- ☐ stand-off pad – whenever needed in poor weather.
- ☐ Free stall housing – number of months indoors / year _____
- ☐ Sacrifice paddock
- ☐ PKE troughs in paddock
- ☐ In-shed feeding

13. Have you started to use of any of these in the last 3 years?

- ☐ feed pads
- ☐ herd home
- ☐ stand-off pad
- ☐ Free stall housing
- ☐ Sacrifice paddock
- ☐ PKE troughs in paddock
- ☐ In-shed feeding
- ☐ Other _____

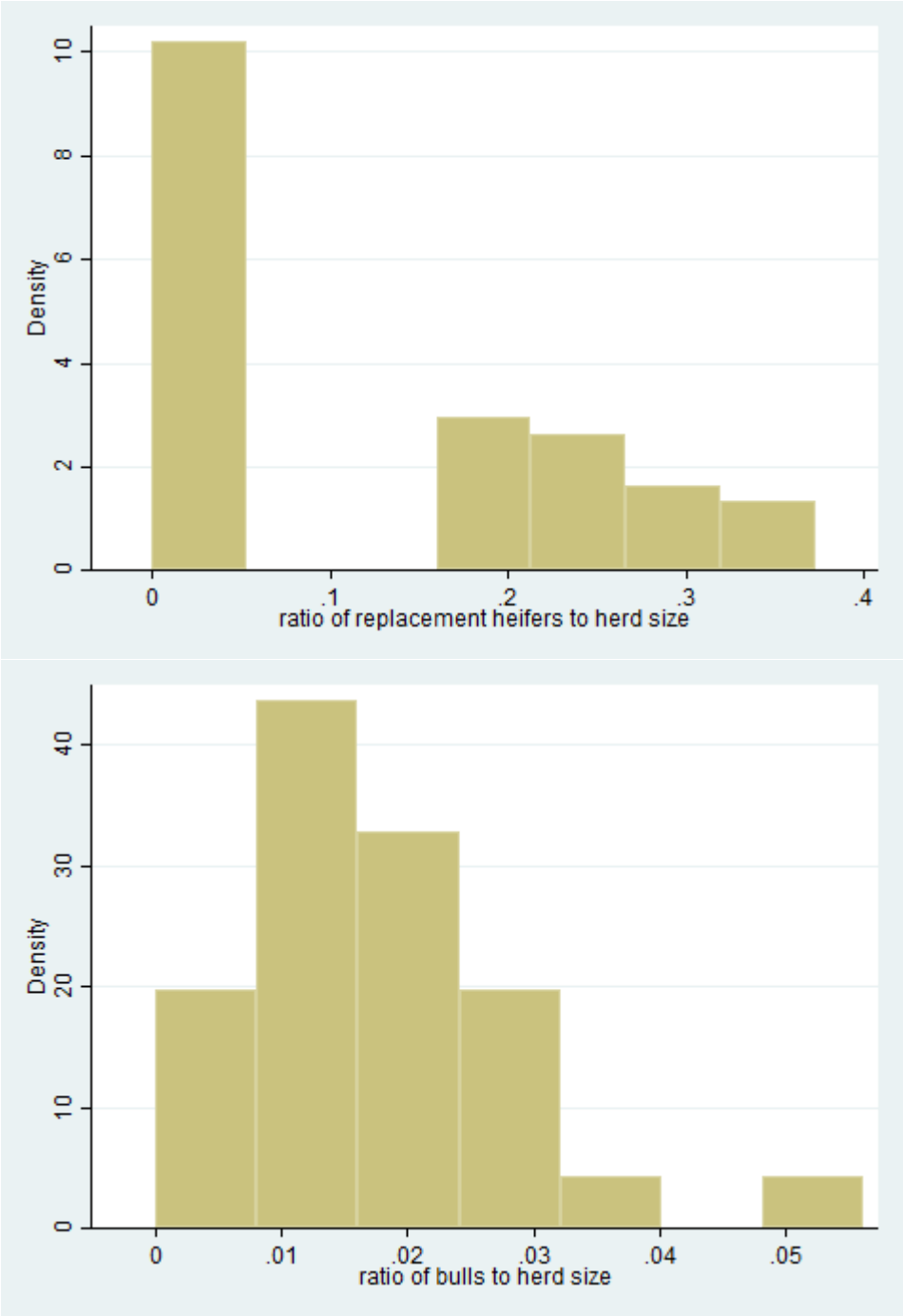
14. Are there any other pieces of information you believe may be relevant to BDD on this farm, or elsewhere?

_____

_____

_____

Supplementary material 2



Supplementary figure 1. Distributions of numbers of heifers/bulls purchased/leased from outside as proportions of a herds.

Appendix 3: Published article: Estimating the herd and cow level prevalence of bovine digital dermatitis on New Zealand dairy farms: A Bayesian superpopulation approach

Appendix 4: Published article: Bayesian analysis of herd-level risk factors for bovine digital dermatitis in New Zealand dairy herds

BMC Veterinary Research

RESEARCH ARTICLE Open Access

Bayesian analysis of herd-level risk factors for bovine digital dermatitis in New Zealand dairy herds

Dan Aaron Yang*, M. Carolyn Gates, Kristina R. Müller and Richard A. Laven

Abstract

Background: Bovine digital dermatitis (BDD) is considered the most important infectious cause of lameness in dairy cattle worldwide, but has only recently been observed in New Zealand. Although many studies have investigated the risk factors for BDD in confined dairy systems, information on risk factors in pasture-based system is limited. Therefore a cross-sectional study including 59,849 animals from 127 dairy herds in four regions of New Zealand was conducted to identify the herd-level factors associated with the probability of a herd being BDD-lesion positive and with within-herd BDD prevalence.

Results: Purchasing heifers was associated with increased odds of a herd being BDD-lesion positive (odds ratio [OR]: 2.33, 95% probability interval [PI]: 1.26–4.42) and a cow being BDD affected (OR: 3.76, 95%PI: 1.73–8.38), respectively. Higher odds of a herd being BDD-lesion positive (OR: 2.06, 95%PI: 1.17–3.62) and a cow being BDD affected (OR: 2.87, 95%PI: 1.43–5.94) were also seen in herds where heifers co-grazed with cattle from other properties. In addition, using outside staff to treat lameness was associated with higher odds of a cow being BDD affected (OR: 2.18, 95%PI: 0.96–4.98).

Conclusion: This study highlighted that movements of heifers are significantly associated with the spread of BDD within and between dairy herds in New Zealand. To minimise the risk of disease introductions in herds where moving heifers cannot be avoided, it is best to purchase heifers only from herds where BDD-freedom has been confirmed and, if heifers have to graze-off a farm, they should be reared as a single biosecure management group, especially since animals may be BDD-infected without having clinically obvious lesions.

Keywords: Digital dermatitis, Dairy cattle, Lameness, Risk factors, Pastoral system, Bayesian, Multilevel modelling

Background

Bovine digital dermatitis (BDD) has been found throughout the world in both confined and pasture-based dairy systems [1, 2]. In many countries, BDD appears to be endemic in dairy herds [3] and is commonly considered as the most important infectious cause of cattle lameness [4]. Clinically, BDD lesions progress or regress through different morphological stages, commonly described using M scores [5, 6]. A rapid BDD lesion detection method such as visual examination during milking is widely used in many studies [7]; although interpretation of such diagnostic outcome is subjective, which usually requires additional validation studies to assess the agreement across the examiners [8].

Multiple studies have evaluated the risk factors associated with BDD prevalence within herds in confined dairy systems. These studies have identified a wide-range of potential risk factors including type of housing [9], using outside staff to trim hooves [10], footbath regimen [11] and access to pasture [12]. In contrast, very few studies [13–15] have been undertaken in cattle that are principally pasture-based with no or very limited use of housing, where many of the risk factors identified in confined animals are irrelevant. Specific research in such systems is essential as there can be large variation between pasture-based dairy herds in the prevalence of BDD [16].

In New Zealand, one previous study has evaluated herd-level risk factors for BDD, but that was undertaken

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in only one region [14]. In that study we used a Bayesian hurdle model to explore the associations between risk factors and BDD prevalence at both the herd and animal levels. The initial separation of the herds into BDD-lesion-free and BDD-lesion positive was based on whether BDD lesions were observed; i.e. a herd with ≥1 lesion was defined as being BDD-lesion positive, otherwise it was defined as being BDD-lesion free [14]. However, simply basing herd status on the presence/absence of visible lesions probably leads to loss of information regarding probability of a herd having BDD and may introduce misclassification bias at the herd level, as there is a chance that a herd where BDD lesions are truly present could be wrongly classified as being BDD-lesion-free due to a combination of limited diagnostic sensitivity and low cow-level prevalence [17].

One method for overcoming this limitation is by using a Bayesian latent class model, which estimates the mean probability of a herd being BDD-lesion positive conditional on the number of test positive animals, the total number of animals tested, and the test characteristics [17]. Thus, the mean probability contains more precise information than the simple dichotomised outcome and increases the power of the study to determine the impact of risk factors on the likelihood of a herd being BDD-lesion positive.

The aim of this study was to use Bayesian methods to investigate the impact of farm management practices on pasture-based dairy herds across New Zealand on 1) the probability of a herd being BDD-lesion positive obtained from a previous Bayesian latent class analysis [16] and 2) the within-herd BDD prevalence, namely the probability of a cow within a herd having BDD lesions.

Methods

Target and source population

The target population was the pasture-based dairy herds in New Zealand and the source population was the herds in the four regions across New Zealand: Waikato and Manawatu in the North Island and the West Coast and Canterbury in the South Island. These regions encompass most of the dairy systems (all grass fed and self-contained; feed imported, either supplement or grazing-off and feed imported to extend lactation) used in New Zealand [16].

Data collection

The dataset was collected as described by Yang et al. [16]. Briefly, the data collection started in the Waikato and moved south following the seasonal pattern of calving to ensure that the great majority of the herds were milking at the herd examinations. In the first phase, half the sampled herds were visited in each region before moving on to the next. In the second phase, the order was reversed, starting in Canterbury and going back north. Within each herd, visual assessment was performed on cows' rear feet in the milking parlour after hosing the feet gently [7].

The farm management practices undertaken in the previous 12 months were collected alongside the visual inspection for BDD using a questionnaire given to the owners or managers of the study herds. The questionnaire was modified by the authors from that used in Yang et al. [14]. The questionnaires were answered after the herd inspection while the first author was still on the farm, so that if the owners or managers were unsure of a question, the first author could explain the intent of the question. The categorical management predictors collected via the questionnaire are shown in Table 1 and a copy of the questionnaire is provided as an additional file (see Additional file 1).

Data processing

The data were imported into Stata 13.1 for cleaning and analysis (StataCorp, USA). One-way tables were used to examine the frequency of responses for each level within the categorical variables. Levels with low frequencies were combined with adjacent levels where biologically plausible. As hoof trimmers were rarely used to trim cows or treat lame cows, this level was combined with using vets to treat lame cows, to create a new dichotomous variable of whether or not the farm had outside staff trimming cows or treating lame cows. Since few farmers reported chemically disinfecting hoof trimming equipment, "chemical disinfection" and "washed by water" were combined to create a new variable of whether or not trimming equipment was cleaned between animals. Since few farmers reported purchasing dairy heifers or cows from saleyards, "saleyards" was combined with "other farms", to create new variables of whether heifers and cows were purchased from outside. Similarly, cow houses were rarely used, so "cow house" was combined with "stand-off pad" and a new variable was created to describe whether the cows were permanently pasture-based (except for milking) or not. All categorical variables included in the final analysis had at least two levels and each level had at least ≥15% of the total responses for the question.

Evaluating seasonal variation

As this was a cross-sectional study, the impact of season on BDD-lesion status and lesion prevalence was not of primary interest. However, as all the data were collected by the first author, it was not possible to complete the data collection in a short time frame and therefore herds were sampled at different points throughout the 2016/2017 lactation season. To confirm that BDD-lesion status and lesion prevalence did not vary significantly

Table 1 Herd-level predictors on BDD collected from 127 New Zealand dairy herds

Variable	Levels	Herds with BDD lesions *N* (%)	Herds without BDD lesions *N* (%)	Total
Type of milking parlour	Rotary	29 (51%)	28 (49%)	57
	Herringbone	34 (49%)	36 (51%)	70
Calving season	Spring only	57 (49%)	59 (51%)	116
	Spring and Autumn	6 (55%)	5 (45%)	11
Whether or not having dairy cattle milking on more than one farm	Yes	9 (14%)	6 (9%)	15
	No	54 (48%)	58 (52%)	112
Source of acquired adult cows (> 2 years old)	Other farms	8 (62%)	5 (38%)	13
	Saleyard	2 (50%)	2 (50%)	4
	Not acquiring	53 (48%)	57 (52%)	110
Source of acquired bulls	Other farms	36 (47%)	41 (53%)	77
	Saleyard	9 (64%)	5 (36%)	14
	Not acquiring	18 (50%)	18 (50%)	36
Source of acquired heifers	Other farms	15 (68%)	7 (32%)	22
	Saleyard	1 (50%)	1 (50%)	2
	Not acquiring	47 (46%)	56 (54%)	103
Whether your calves/heifers co-grazing with calves/heifers from other farms	Yes	46 (59%)	32 (41%)	78
	No	17 (35%)	32 (65%)	49
Whether your milking dairy cattle co-grazing with cows from other farms in winter	Yes	28 (57%)	21 (43%)	49
	No	35 (45%)	43 (55%)	78
Providing grazing for stock from other farms at your farm or not	Yes	3 (50%)	3 (50%)	6
	No	60 (50%)	61 (50%)	121
Using a transport company to transport animals (not for slaughter) or not	Yes	43 (49%)	45 (51%)	88
	No	20 (51%)	19 (49%)	39
Share a loading ramp or not	Yes	7 (41%)	10 (59%)	17
	No	56 (51%)	54 (49%)	110
Who did most of the hoof trimming/ lame cattle treatment on your farm	Vet	7 (39%)	11 (61%)	18
	Hoof trimmer	6 (86%)	1 (14%)	7
	On-farm staff	50 (49%)	52 (51%)	102
Trimming equipment cleaning methods	Washed by water	28 (51%)	27 (49%)	55
	Chemically disinfected	11 (55%)	9 (45%)	20
	Not wash	24 (46%)	28 (54%)	52
Use a footbath or not	Yes	10 (63%)	6 (37%)	16
	No	53 (48%)	58 (52%)	111
Whether or not use stand-off pads or cow houses in winter or poor weather	Stand-off pad	18 (49%)	19 (51%)	37
	Cow house	2 (22%)	7 (78%)	9
	Neither	43 (53%)	38 (47%)	81
Main material of the walking track/race from paddock to the milking parlour	Gravel	22 (35%)	40 (65%)	62
	Concrete	1 (50%)	1 (50%)	2
	Other	40 (63%)	23 (37%)	63
Use feedpad or not	Yes	23 (48%)	25 (52%)	48
	No	40 (51%)	39 (49%)	79

BDD, bovine digital dermatitis; *N* (%), numbers of herds having such a predictor (row percentage of herds having such a predictor)
Average herd milk solid production in BDD-lesion positive/negative herds were 414.9 kg/cow year and 414.1 kg/cow year, respectively

between different months, generalized estimating equations [18] and beta regression models were respectively used to examine whether the average cow-level prevalence or probabilities of a herd being BDD-lesion positive differed significantly between months in Waikato and Manawatu regions. This process was not applied to Canterbury since 18/19 herds were visited in the same month.

Univariable models

For the two outcome variables (within-herd prevalence and probability of a herd being BDD-lesion positive), univariable logistic regression models and univariable beta regression models in the frequentist framework were respectively used to select predictors for fitting in the multivariable models. Any predictors with p-value ≤0.2 were included in the further analyses.

Multivariable model 1

This analysis was designed to quantify the strength of associations between farm management practices and within-herd prevalence. A Bayesian binomial model was constructed. The model was built using a forward stepwise strategy. The predictors were retained in the model when the 90% probability intervals of their corresponding regression coefficients did not overlap 0. If inclusion of a predictor altered the coefficient of any of the existing predictors by > 15%; the newly included predictor was considered as a confounder and was forced into the model regardless its 90% probability interval [19]. Once the preliminary main effect model was constructed, two-way interactions between all predictors in the model were created. An interaction term was retained if its 95% probability interval excluded 0. The final model structure is presented below:

$$\begin{aligned} y_j &\sim binomial\left(p_j,\ n_j\right) \\ \text{logit}\left(p_j\right) &= \beta_0 + \beta_1 x_j + \beta_2 g_j + \beta_3 h_j + U_{region(j)} \\ &\quad + W_j U_{region(j)} \sim N(0,\ \sigma_U) W_j \sim N(0,\ \sigma_W) \end{aligned} \tag{1}$$

where y_j was the number of the cows with visible BDD lesions in the j^{th} herd of all the regions, which was modelled using a binomial distribution with the parameters: the proportion of cows with visible lesions (p_j) and number of cows being examined (n_j); β_0 was the intercept, β_1, β_2 and β_3 were the regression coefficients for the predictors x_j, g_j and h_j which represented whether heifers were purchased from outside sources, whether heifers were co-grazed with heifers from other farms and whether outside personnel treated lame cows. Finally, $U_{region(j)}$, W_j were the random effects at regional and herd level, respectively and modelled using two independent normal distributions with zero means and standard deviations σ_U and σ_W.

The choice of prior distributions contributes to the posterior distributions, thus utilising informative priors results in better inferences compared to "vague" priors [20]. It is difficult to place informative priors for the regression coefficients. However, such priors can be indirectly induced to define probabilities for different combinations of predictors. Partially informative priors were assigned to β_0, β_1 and β_2. First, the proportion of cows with visible lesions (prevalence) in a "typical" closed herd was defined as $\tilde{p}_0$. This meant $x = 0$, $g = 0$ and $h = 0$. Therefore, according to Eq. 1, $\beta_0 = \text{logit}\,(\tilde{p}_0)$. Second, specify $\tilde{p}_1$ as the prevalence of a herd where some heifers were purchased from outside, in this case, $x = 1$, but $g = 0$ and $h = 0$. Thus, $\beta_1 = \text{logit}\,(\tilde{p}_1) - \beta_0$. Finally, let $\tilde{p}_2$ denote the prevalence of a herd which contained purchased heifers, and, at the same time, sent its own heifers to co-graze with heifers from other farms ($x = 1$ and $g = 1$, but $h = 0$). This gave $\beta_2 = \text{logit}\,(\tilde{p}_2) - \text{logit}\,(\tilde{p}_1)$. Logit-normal distribution was used for these prevalence priors. Below we use $\tilde{p}_0$ as an example to illustrate the way to convert a prevalence estimate to its corresponding logit-normal distribution such as $\text{logit}\,(\tilde{p}_0) \sim N(\mu_{\beta 0}, \tau_{\beta 0})$, where τ is the precision term defined as the reciprocal of the variance. Our best estimate of the prevalence in a closed herd was m_0 and we were 95% confident that it was less than l_0; then $\mu_{\beta 0} = \text{logit}(m_0)$. The standard deviation $\sigma_{\beta 0} = [\text{logit}(l_0) - \text{logit}(m_0)]/1.645$, eventually $\tau_{\beta 0} = 1/\sigma_{\beta 0}^2$.

The best estimates of $\tilde{p}_0$, $\tilde{p}_1$ and $\tilde{p}_2$ came from the previous analyses of BDD data in Taranaki and the authors' expert opinion. One important observation was that in contrast to previous studies of housed cattle, the apparent cow-level prevalence of BDD was very low (mean = 1.2%, Yang et al. [1]) with 26.8% of herds having fewer than1% of cows with observed lesions. In Canterbury region, where median herd size was 840 and > 21% of herds had ≥1000 cows; we were able to detect BDD at an apparent within-herd prevalence of 0.1% (i.e. one cow with lesions in a 1000-cow herd). Thus to reflect our belief that a closed herd was likely to have no or extremely rare BDD lesions, we took 0.05% as our "best point estimate" for $\tilde{p}_0$. Furthermore we were also 95% confident that it was less than 0.35%, i.e., one cow with BDD lesion(s) in a 300-cow herd. Based on the method described in the last paragraph, this led to $\mu_{\beta 0} = -7.6$ and $\tau_{\beta 0} = 0.71$. Table 2 summarises our "best estimates" for $\tilde{p}_0$, $\tilde{p}_1$ and $\tilde{p}_2$. Uniform priors (0, 3) and (0, 2) were set for σ_U and σ_W, respectively. This reflected our belief that the variability of herd-level prevalence across regions was bigger than the variability across herds. However, the parameter values assigned to the uniform priors were considered to be non-specific as

Table 2 The "best estimates" for within-herd prevalence ($\tilde{p}_k$) of BDD conditional on the different covariates

			Prevalence	
	Purchasing heifers	Heifers co-grazing	prior mode	95th percentile
$\tilde{p}_0$	No	No	0.05%	0.35%
$\tilde{p}_1$	Yes	No	0.2%	1%
$\tilde{p}_2$	Yes	Yes	0.5%	3%

BDD, bovine digital dermatitis

we did not know the standard deviations of the two random effects.

Under the partially informative priors, the fit of the model to the data was evaluated using posterior predictive checks which compared the observed outcome data to the data simulated/predicted by the posterior predictive distribution [21]. The Bayesian *P*-value quantifies the probability that the discrepancy between the predicted and observed values. A Bayesian P-value close to 0.50 indicates adequate model fit, although a value between 0.20 and 0.80 is also accepted [22].

Sensitivity analysis was used to assess the sensitivity of the posteriors to the priors. Table 3 summarises the distributions of the model priors and the priors used for the sensitivity analysis. The model was developed using OpenBUGS [23]. Posterior inferences were obtained using Markov chain Monte Carlo (MCMC) approximation. The posterior distribution of each parameter was reported using median and 95% probability interval (PI). After discarding the first 10,000 iterations as burn-in period, the model was further run for 100,000 iterations. Convergence was assessed using BGR-plots by running three chains with different sets of initial values [24].

Multivariable model 2

This analysis was designed to assess the associations between farm management predictors and the probability of herd being BDD-lesion positive (PP). This analysis did not include herds on the West Coast as the region was determined to be free of the disease [16].

The data were modelled using a Bayesian beta model [25]. π_k was used to denote the PP_k for k^{th} herd . The variable "region" was initially modelled as a random effect $V_{region(k)} \sim N(0, \frac{1}{\sqrt{\tau_V}})$, where τ_V was the precision term. The model was constructed as follows:

$$\pi_k \sim Beta(a_k, b_k)$$

$$a_k = \mu_k \phi \quad (2)$$

$$b_k = \phi(1-\mu_k) \quad (3)$$

$$\text{logit}(\mu_k) = \gamma z_k + V_{region\,(k)} \quad (4)$$

$$V_{region(k)} \sim N\left(0, \frac{1}{\sqrt{\tau_V}}\right)$$

where z_k was the predictor vector, γ denoted the regression coefficient vector and μ_k the mean and ϕ a measure of variability, with a larger value of ϕ indicating less variability [26].

Diffuse normal distributions (mean = 0, precision = 0.01) were set for all the regression coefficients, and a vague gamma distribution (1, 1) was set for ϕ and τ_V. The model was built using a forward stepwise strategy. Predictors were retained if the 90% probability interval for the regression coefficients excluded 0. Confounders were assessed using the method described as per Multivariable model 1. Two-way interactions between all predictors in model were investigated after building the main effect model. Inclusion criteria for an interaction term were the same as for Multivariable model 1. In this model, the linear predictor was the log-odds. The odds were defined as the probability of a herd being BDD-lesion positive divided by the probability of a herd being BDD-lesion-negative at each level of a predictor. The model was therefore able to identify any farm management practice associated with higher odds of being BDD-lesion positive for a randomly selected herd in any BDD-affected region.

Table 3 The prior distributions for parameters used in the Bayesian multilevel multivariable binomial model

Parameter	Main analysis	Sensitivity analysis scenarios		
		1	2	3
β_0	*N* (−7.6, 0.71)	*N* (−5, 0.001)	*N* (−7.6, 0.71)	*N* (−7.6, 0.71)
β_1	$\text{logit}(\tilde{p}_1)-\beta_0$	*N* (0, 0.001)	$\text{logit}(\tilde{p}_1)-\beta_0$	$\text{logit}(\tilde{p}_1)-\beta_0$
β_2	$\text{logit}(\tilde{p}_2)-\text{logit}(\tilde{p}_1)$	*N* (0, 0.001)	$\text{logit}(\tilde{p}_2)-\text{logit}(\tilde{p}_1)$	$\text{logit}(\tilde{p}_2)-\text{logit}(\tilde{p}_1)$
β_3	*N* (0, 0.001)	*N* (0, 0.001)	*N* (0, 0.001)	*N* (0, 0.001)
σ_U	Uniform (0, 3)	Uniform (0, 3)	Uniform (0, 5)	Uniform (0, 9)
σ_W	Uniform (0, 2)	Uniform (0, 2)	Uniform (0, 3)	Uniform (0, 2)

β_0, intercept; β_1, purchasing heifers; β_2, heifers co-grazing; β_3, lameness treated by outside staff
σ_U and σ_W, standard deviation of random effects at region and herd levels
$\tilde{p}_1$ ~ logit-normal (−6.21, 1.03); $\tilde{p}_2$ ~ logit-normal (−5.29, 0.82)

Multivariable model 3

Although the mixed effects beta model modelled the overall variability of the probability in different regions; it was not able to describe the difference between particular regions, therefore we also built a model which treated "region" as a fixed effect. Assuming the model had in total t farm management practices, Eq. (4) was changed to:

$$\text{logit}(\mu_k) = \gamma_c z_{ck} + \gamma_w z_{wk} + \gamma_1 z_{1k} + \ldots + \gamma_t z_{tk} \qquad (5)$$

with $V_{region(k)} \sim N(0, \frac{1}{\sqrt{\tau_V}})$ dropped. Here, z_{ck} and z_{wk} were the dummy variables for the regions Canterbury and Waikato (level "Manawatu" was treated as reference level). This fixed effects model can be used to predict the probability of a herd being BDD-lesion positive with different covariates in any particular region.

The deviance information criteria (DIC) of both beta models were compared. In addition, a global measure of variation explained by each of the beta models was obtained by computing pseudo-R^2 defined as the squared correlation between the linear predictor and the logit-transformed outcome variable [27]. Both beta models were developed using OpenBUGS [23]. After discarding the first 5000 iterations as the burn-in period, the model was further run for 100,000 iterations. Convergence was assessed using BGR-plots by running three chains with different sets of initial values [24]. The OpenBUGS code for Multivariable model 1, 2 and 3 is provided as an additional file (see Additional file 2).

Results

There was no evidence to support seasonal differences in any of the outcome variables. In Waikato region, the average cow-level prevalences in September 2016 and in January 2017 were not significantly different ($P = 0.94$). The probabilities of BDD-lesion positive also did not differ significantly between these two months ($P = 0.65$). In Manawatu, the average cow-level prevalences in September ($P = 0.46$) and November ($P = 0.22$) were not significantly different to that in December. Similarly, significant differences in the probabilities of BDD-lesion positive in September ($P = 0.86$), November ($P = 0.28$) and December were not evident. These findings ruled out the potential seasonal impact on BDD prevalences in this study. Table 4 displays the total herds and animals sampled as well as the proportions of herds/animals having BDD lesions in each region during the data collecting period.

The outputs from the Bayesian binomial model (Multivariable model 1) with our partially informative priors are shown in Table 5. Lack of model fit was not evident (Bayesian P-value = 0.5). The posteriors for β_1, β_2 and β_3 were robust in all sensitivity analysis scenarios. The posterior median for β_0 increased slightly (− 8.05 vs. − 7.67) and its 95%PI was also wider (− 10.65, − 5.707) given the diffuse prior N (− 5, 0.001) rather than the informative prior. The posterior for σ_W was not sensitive to its prior, although the posterior for σ_U was sensitive to its prior. The posterior median of σ_U increased from 2.4 to 3.2 when the prior changed from Uniform (0, 3) to Uniform (0, 5). It further increased to 4 if the prior changed to Uniform (0, 9). Nevertheless, there was no impact on the posteriors for the regression coefficients. The results of the sensitivity analyses are provided as an additional file (see Additional file 3).

Based on Multivariable model 1, cattle in a herd which purchased heifers from outside were more likely to have BDD lesions than cattle in a herd that did not purchase heifers (OR: 3.76, 95%PI: 1.73–8.38). Being in a herd which co-grazed heifers with animals from other properties also increased the odds of a cow having BDD lesions (OR: 2.87, 95%PI: 1.43–5.94). The use of outside staff to treat lameness was found to be associated with the increased within-herd prevalence (OR: 2.18, 95%PI: 0.96–4.98).

Except for the intercepts, the posteriors for the parameters reported by the Bayesian mixed effects beta model and fixed effects beta model were nearly identical. Table 6 summarises the models' outputs. The DIC for each model was also very similar, − 533.3 for the fixed effects model and − 533.5 for the mixed effects model. Two farm management practices were identified as being significantly associated with the odds of a herd being BDD-lesion positive. Based on the mixed effects beta model, the odds of a herd being BDD-lesion positive was 2.33 times (95%PI: 1.26–4.42) higher in a herd with purchased heifers compared to one without, and 2.06 times

Table 4 Total (#) herds/cattle sampled, proportions (%) of herds/cattle with BDD lesions detected in each region

	Region			
Parameters	Waikato	Manawatu	The West Coast	South Canterbury
# of herds	40	41	27	19
# and % of affected herds	34 (85%)	15 (37%)	0	14 (74%)
# of cows	15,522	15,546	12,978	15,803
# and % affected cows	241 (1.6%)	68 (0.4%)	0	337 (2.1%)

BDD bovine digital dermatitis

Table 5 The posterior distributions for parameters of the Bayesian multilevel multivariable binomial model

Parameter	Interpretation	Posterior distribution		
		Median	2.5th Percentile	97.5th Percentile
β_0	Intercept	-7.67	−8.9	−6.46
β_1	Purchasing heifers	1.32	0.55	2.13
β_2	Heifers co-grazing	1.06	0.36	1.78
β_3	Lameness treated by outside staff	0.78	−0.04	1.61
σ_U	Region level random effect	2.36	1.33	2.97
σ_W	Herd level random effect	1.41	1.12	1.8

(95%PI: 1.17–3.62) higher if heifers co-grazed with cattle from other properties. The predicted probabilities from the fixed effects model of a herd being BDD-lesion positive conditional on different farm management practices and region are displayed in Fig. 1. However, 74% of the variation in the probability of a herd being BDD-lesion positive remained unexplained by either beta model (pseudo-R^2 = 0.26).

Discussion

This study found that both co-grazing with heifers from other properties and purchasing heifers from other farms were associated with an increased probability of a herd being BDD-lesion positive as well as increased within-herd prevalence. Our previous study [14] also found that that youngstock movement between farms considerably increased the probability of a farm having at least one visible lesion (OR: 4.15, 95%PI: 1.39–15.27). Compared to Yang et al. [14], our current study evaluated youngstock movement in a more detailed way by dividing such movements into heifer purchasing and heifer co-grazing. Unlike Yang et al. [14] who reported that youngstock movement affected only a herd's probability of having at least one cow with BDD lesions but not within-herd prevalence, this broader-scale study (along with the more detailed way of recording the predictors) found that youngstock movement increased both the probability of a herd being BDD-lesion positive and the within-herd prevalence. The likely inference is that heifers act as a reservoir for BDD transmission between dairy herds and between cows within herds in New Zealand [28]. In contrast, both this analysis and Yang et al. [14] found no effect of purchasing adult cattle on BDD risk. This lack of effect is most likely due to the much smaller numbers of purchased adult cows compared to the numbers of heifers purchased for replacement [13, 14].

Table 6 The posterior distributions for parameters of the Bayesian beta models

Parameter		Posterior distribution		
		Median	2.5th Percentile	97.5th Percentile
Mixed effects beta model				
γ_0	Intercept	0.07	−1.13	1.36
γ_1	Heifers co-grazing	0.73	0.16	1.29
γ_2	Purchasing heifers	0.85	0.23	1.49
φ		0.53	0.42	0.66
τ_V		1.43	0.22	4.81
Fixed effects beta model				
γ_0	Intercept	−0.38	−0.93	0.16
γ_1	Heifers co-grazing	0.72	0.15	1.28
γ_2	Purchasing heifers	0.84	0.22	1.48
γ_c	Canterbury	0.82	0.11	1.55
γ_w	Waikato	0.50	−0.08	1.09
φ		0.53	0.42	0.66

$\varphi = a + b$, where a and b are shape parameters of a beta distribution
τ_V, precision term of the region level random effect defined as 1/variance

Yang et al. [14] reported that herds with a rotary platform were more likely to have at least one cow with BDD lesions than herds with a herringbone (OR: 3.19, 95%PI: 1.31–8.51), though as with heifer movement, no effect was seen on within-herd prevalence. This may have been due to the ease of finding at least one lesion in herds with rotary platforms rather than being an actual risk factor [14]. Our current analysis did not include parlour type in the final model as the analysis found it to be neither statistically significant nor a confounder.

Two New Zealand studies [14, 15] reported that on BDD-positive farms, the within-herd prevalence was higher on farms where the outside staff came for hoof trimming (prevalence ratio [PR]: 3.13, 95%PI: 1.25–7.29 and risk ratio [RR]: 2.06, 95% confidence interval [CI]: 1.05–4.06). Although our current analysis did not confirm this finding, the calculated OR 2.18 was still in the realm considered to be biologically important [10] and the 95%PI: 0.96–4.98 only just included 1. It is not entirely clear how these effects could be mediated under New Zealand conditions. The use of outside staff for lame cows is typically unrelated to BDD since BDD rarely causes lameness in New Zealand dairy cattle. However, failure to clean trimming equipment properly between cows and between herds could represent a mechanism for spread [14]. To confirm this hypothesis, our current study included whether trimming equipment was cleaned between cows as a potential risk factor. However, no effect of cleaning/washing equipment between cows was found; this suggests that if there is an effect of outside staff on the within-herd prevalence of BDD that it is not mediated via dirty equipment. Further research is required to better estimate the impact of

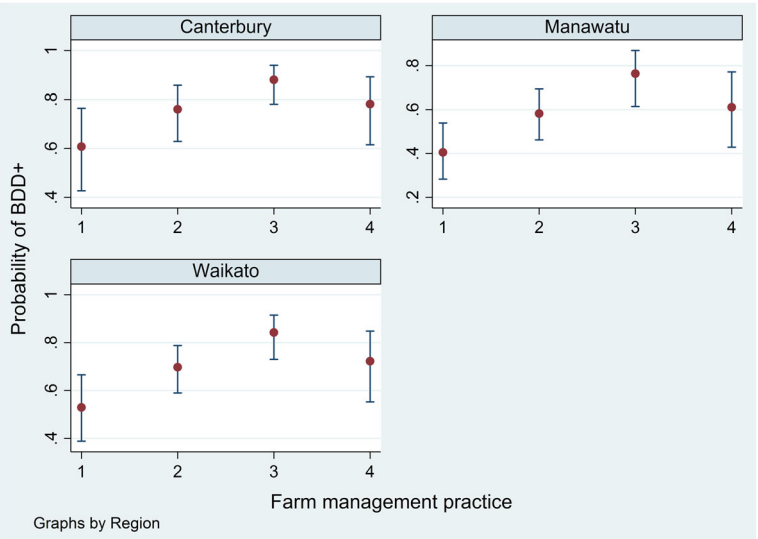

Fig. 1 Predicted probability of a herd being BDD-lesion positive given different farm management practices. 1 = a closed herd, 2 = a herd having heifers co-grazing with animals from other properties only, 3 = a herd having heifers co-grazing with animals from other properties and having purchased heifers, 4 = a herd having purchased heifers only; BDD = bovine digital dermatitis

using outside staff to treat lame cows on BDD prevalence and to investigate potential pathways by which such an effect could be mediated.

The only other study of risk factors for BDD in pasture-based cows is that by Rodriguez-Lainz et al. [13]. However, of the 22 farms in that study only 2 kept their cattle at pasture all year round, with 13/22 keeping cattle in an open corral or loose yard for at least part of the year, whereas in this study, all 127 farms grazed their cattle throughout the year. As such many of the factors analysed by Rodriguez-Lainz et al. [13] (e.g. housing type and season of calving) are not directly relevant to the New Zealand situation and thus not included in our analysis. Although it is difficult to directly compare the study findings, Rodriguez-Lainz et al. [13] did find that there was an effect of purchasing replacement heifers on within-herd prevalence of BDD (OR: 3.16, 95%CI: 1.61–6.21), but not purchasing adult cows (OR: 1.31, 95% CI: 0.72–2.38). The data from Rodriguez-Lainz et al. [13] provided no evidence as to whether, in pasture-based cattle, using outside staff to trim feet increases the within-herd prevalence of BDD as in that study all cattle were treated or trimmed by farm staff. However, using hoof trimmers who operated on multiple farms was found to be significantly associated with higher BDD within-herd incidence in housed cattle (OR: 2.8, 95% CI: 1.9–4.2) [10].

Many studies on dairy cattle from intensive housing systems in the northern hemisphere have also identified herd-level risk factors for this disease. Decreasing the access to pasture was found to increase the risk of BDD [12, 29, 30]. The type of housing for animals was also associated with BDD prevalence, i.e. cows that housed in cubicles had higher BDD prevalence and more severe BDD cases [31] than cows in straw yards, which also agreed with Onyiro et al. [9]. In cubicles houses, the size of cubicles was linked to the risk of BDD [29]. This is because cows tend to spend longer time standing in shorter and narrower cubicles; therefore the contact between heels and slurry was increased [32]. However, these factors tend not to be an issue in New Zealand pasture-based systems and were therefore not included in the current study. It could be interesting in future studies to evaluate cleanliness of legs in cattle since higher prevalence of BDD had been found in cows with dirty legs [33]. This is one possible explanation why no BDD lesions were seen on the West Coast where the cows' feet were generally much cleaner compared to other regions.

The results of this study show that even in New Zealand where BDD prevalence is very low, heifers are the most likely source of disease spread between and within herds. Particular care should be taken when purchasing heifers as replacement animals and ideally, replacement heifers should only be purchased from herds where BDD-freedom has been confirmed. The latter may be difficult in New Zealand since many heifers are purchased in late-autumn when cows are not being milked and it is therefore not possible to observe the milking herd for BDD. In such cases, visual inspection of the whole heifer group (not just the heifers for purchase) is a potential alternative to increase the probability of finding at least one animal with BDD lesions. If any of the heifers have visible lesion(s), then the entire group should not be purchased

as animals can still be infected with BDD in the absence of visible lesions [34]. Where heifers are co-grazing with animals from multiple herds, it becomes much more difficult to ensure that co-grazing heifers will not come in contact with BDD infected cattle, although little is currently known about the transmission dynamics of BDD in grazed dry stock. Thus, the only reliable method to ensure that heifers grazed away from the farm do not become infected with BDD is to require that they are grazed as a single biosecure management group. This is important to prevent the spread of many infectious diseases as well as BDD.

Bayesian methods were adopted as the analytical approach in this paper. Bayesian analyses incorporate previous scientific understanding, e.g. such as the likely association between a farm management practice and BDD within-herd prevalence, into analysis (see Multivariable model 1), so that the inference (i.e. the posterior distribution) is based on both the data and our prior information. This is in contrast to other methods which typically ignore such previous understanding [35]. Furthermore even if previous information of a research question is not available, the Bayesian methods still has significant advantages such as being able to directly compare the relative probabilities of two or more hypotheses rather than simply using the probability of the data given the null hypothesis to determine whether an alternative hypothesis was plausible.

Multivariable model 2 and 3 used uniform priors, as this was the first use of beta models to study risk factors on the herd-level BDD outcome estimated from a previous Bayesian latent class analysis. This use of the outcome from the latent class analysis reduced the likelihood of misclassification errors at the herd level, as the effect of diagnostic sensitivity and specificity on the herd level diagnosis was factored into the latent class model [16].

Although misclassification bias has been adjusted at the herd level in Multivariable model 2 and 3, our Multivariable model 1 did not account for animal level misclassifications. This could potentially have influenced the analysis of risk factors affecting within-herd prevalence. Misclassification at the individual level, as at the herd level, can be minimised by incorporating the known sensitivity and specificity of a diagnostic method [36]. However, when the impact of specificity and sensitivity on the diagnosis of BDD in the individual animal was included during the modelling process, it resulted in non-convergence of the Markov chains. This may be related to the model being non-identifiable. Using a more sensitive detection method inspecting lifted cows' feet in the trimming chute, would have decreased any potential impact but would have been cost prohibitive [7].

The other limitation was that Multivariable models 2 and 3 explained only 26% of the variation in the probability of a herd being BDD-positive. This indicates that further investigation of more factors which could potentially affect the probability of herd being BDD-lesion positive was required.

Conclusions

Our study investigated potential risk factors for BDD across New Zealand and identified that purchasing replacement heifers and co-grazing heifers with animals from other herds were significantly associated with a higher probability of a herd being BDD-lesion positive and higher within-herd prevalence of BDD. This is consistent with previous findings from pasture-based systems. However, the identified risk factors only explained a small proportion of the variation in probability of a herd being BDD-lesion positive. Our study also found that using outside staff for trimming had a large effect on within-herd prevalence (doubling the odds of an individual cow having BDD). Given that we can't rule out the possibility of contaminated hoof trimming equipment contributing to the between-herd spread of BDD, it would be advisable for farms to maintain their own set of equipment. Further research should be undertaken to better estimate the impact of this factor on BDD and how it can be mediated through different biosecurity interventions.

Additional files

Additional file 1: The questionnaire used to collect farm management practices. (DOCX 176 kb)

Additional file 2: OpenBUGS code for the three Bayesian multivariable models used in this study. (DOCX 19 kb)

Additional file 3: Results of the sensitivity analysis for Multivariable model 1. (DOCX 18 kb)

Abbreviations

BDD: Bovine digital dermatitis; CI: Confidence interval; DIC: Deviance information criteria; MCMC: Markov chain Monte Carlo; OR: Odds ratio; PI: Probability interval; PP: Probability of herd being BDD-lesion positive; PR: Prevalence ratio; RR: Risk ratio

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Availability of data and materials
The subset of the data was available in Additional file 2. The full data collected and analysed during the current study are not publicly available as they contain confidential information of the participated farmers. However, the datasets are available from the corresponding author on reasonable request.

Authors' contributions
DAY, KRM and RAL participated in the study design and coordination. DAY collected the data and analysed the data. DAY, MCG and RAL contributed to the manuscript. All authors were involved in the manuscript preparation and approved the final manuscript.

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Prof Laven is a professor in production animal health and welfare.

Ethics approval and consent to participate
The New Zealand Animal Welfare Act (1999) states that if an animal is subject to a manipulation, it needs ethics approval.
Section three of this act defines a manipulation as follows:
In this Act, unless the context otherwise requires, the term manipulation, in relation to an animal, means, subject to subsections (1A) to (3), interfering with the normal physiological, behavioural, or anatomical integrity of the animal by deliberately—.
(a) subjecting it to a procedure which is unusual or abnormal when compared with that to which animals of that type would be subjected under normal management or practice and which involves—.
(i) exposing the animal to any parasite, micro-organism, drug, chemical, biological product, radiation, electrical stimulation, or environmental condition; or.
(ii) enforced activity, restraint, nutrition, or surgical intervention; or.
(b) depriving the animal of usual care;—.
As washing of feet to observe BDD is normal management and the animals were observed during milking (so there is no restraint beyond normal) what was done does not meet the definition of a manipulation.
The farm owners were identified by local veterinary practices and verbal agreement was obtained prior to visiting farms.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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Bovine Digital Dermatitis in cattle:
Confidential farm management questionnaire

2016-2017

This questionnaire should take 15-20 minutes to complete and your cooperation is much appreciated. This survey is being performed in conjunction with a herd screening for Bovine Digital Dermatitis (BDD). The aims are to describe management practices that may be relevant to BDD.

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For any queries, please contact d.yang@massey.ac.nz

BDD in New Zealand

BDD has not been observed in New Zealand until 2004. From 2004 to 2011, sporadic cases were reported to Ministry for Primary Industries. In 2014, a large scale cross-sectional survey in Taranaki raised awareness of the disease. There were no outbreaks in any herd but more than 60% of herds were infected. The concern is that the disease may start spreading as it has done elsewhere in the world and contribute to incidence of lameness on farm. We therefore urgently require more information of this disease across the country to investigate the prevalence and to identify farm management practices which could at some point trigger epidemic outbreaks of BDD.

To date, we do not have a strong scientific understanding of the dynamics of the disease. Our objectives are to

- provide scientifically-based evidence to assess whether the disease is spreading or becoming more common in New Zealand;
- characterise the cases identified in New Zealand, and describe the patterns of disease within herds;
- develop relevant protocols and recommendations for identifying, treating and controlling the disease.

Confidentiality

All information given will be treated with confidentiality. The farm details recorded on this page will be accessible to the principal researchers only. We will not contact you without your consent, and even if given, will not contact you unless necessary.

Farm details

1. Please complete the following contact details:

Name and farm address	_____ _____ _____
Email address	_____
Farm telephone / mobile	Tel. _____ Mobile_____
FarmsOnLine number (if applicable)	_____
Person completing the questionnaire	☐ farm owner(s) ☐ farm manager(s) ☐ stockperson(s) ☐ other: _____
Date of completion	____ / ____ / _____
Veterinary practice	_____

2. Which region are you in?
- ☐ Waikato
- ☐ Manawatu
- ☐ Canterbury
- ☐ West Coast

3. **How many animals** were you milking on the day of the screening visit?

Type	**Number milked on date of screening**
Dairy heifers	
Dairy cows (>2 years old)	

4. What type of milking shed do you have?
- ☐ rotary
- ☐ herringbone

Lactation related

5. What is the **major** calving season of your herd?
- ☐ spring
- ☐ autumn
- ☐ both

6. What is your planned start of calving?

_____

7. Can you estimate the average **herd milk production** (MS/cow year) approximately **in the last 12 months**?

_____

Cattle movement

8. Do you have dairy cattle milking on **more than one farm**?
- ☐ yes, there is **movement** of these milking cattle between the farms I work on
- ☐ yes, but the cattle do not move
- ☐ no

9. Did you purchase any animals into your milking herd from outside **in the last 12 months**? If yes, where did you bring the following animals onto this farm?

Category	**Major source of acquired animals**
Dairy heifers	□ no I did not □ directly from other farm(s) □ sale yards
Dairy cows (>2 years old)	□ no I did not □ directly from other farm(s) □ sale yards
Breeding bulls	□ no I did not □ directly from other farm(s) □ sale yards

10. Do your **calves** go away grazing off your farm(s)?

- □ yes mixed with calves from other farm(s)
- □ yes but not with calves from other farm(s)
- □ no

11. Do your **milking dairy cattle** go away grazing in winter?

- □ yes mixed with dairy cattle from other farm(s)
- □ yes but not with dairy cattle from other farm(s)
- □ no

12. Do you provide grazing for stock from other farms at your farm?

- □ yes
- □ no

13. Have you used a transport company to transport animals (not for slaughter) **in the last 12 months**?

- □ yes
- □ no

14. Do you share a loading ramp with another farm(s)?

- □ yes
- □ no

Hoof care

15. **Who** did most of the hoof trimming/ lame cattle treatment on your farm?
    - □ yourself /farm staff
    - □ vet
    - □ hoof trimmer

16. Was hoof trimming equipment routinely **washed** with water between cattle?
    - □ yes
    - □ no

17. Was hoof trimming equipment routinely **chemically disinfected** between cattle?
    - □ yes
    - □ no

18. How often do you **use** a footbath?
    - □ never
    - □ sometimes
    - □ the whole lactation

19. How often do you **change the contents** of the footbath?

_____

Farm management

20. Which type of land did your lactating cattle access in winter or whenever the weather was poor (you can tick more than one option)?
    - □ pasture
    - □ stand-off pads, number of months / year_____
    - □ barns or cow houses, number of months / year_____

21. What is the main material your cattle walk on to get from the paddock to the shed?
    - □ pasture, mud
    - □ stones
    - □ concrete
    - □ other _____

22. Did you use a feed pad?
    - □ yes
    - □ no

Lameness history

23. How many lame cows were on your farm **in the last 12 months**?

_____

24. What was the most common reason for lameness on your farm **in the last 12 months**?

- □ white line disease
- □ foot rot
- □ sole damage
- □ other _____

Additional file 2 for Yang DA, Gates MC, Müller KR and Laven RA. "Bayesian analysis of herd-level risk factors for bovine digital dermatitis in New Zealand dairy herds". BMC Vet Research.

OpenBUGS code for multilevel mixed effects binomial model

```
model{
for(k in 1:4) { u1[k] ~ dnorm(0, tau1) }   #specify region level random effect
tau1<-1/sigma1/sigma1        #tau1 is the precision = 1/variance
sigma1~dunif(0,3)            #sigma1 is the SD, prior for it

for(i in 1:127) {
y[i]~dbin(p[i],hs[i])            #lesion ~ binomial dist with prev and herd size
#heifer: buying heifers
#calfgrz: heifers co-grazing
#hf: lameness treated by outside staff
logit(p[i])<-b0+b[1]*heifer[i]+b[2]*calfgrz[i]+b[3]*hf[i]+u1[region[i]]+u2[i]
u2[i]~dnorm(0,tau2)        #random effect at herd level
}

tau2<-1/sigma2/sigma2
sigma2~dunif(0,2)                #same way as tau1, sigma1

#real priors
b0~dnorm(-7.600402, 0.712435)              #logit(0.0005),0.0035
b[1]<-logitnorm[1]-b0
b[2]<-logitnorm[2]-b[1]-b0
b[3]~dnorm(0,0.001)
logitnorm[1]~dnorm(-6.21261, 1.03431)   #0.002, 0.01
logitnorm[2]~dnorm(-5.2933, 0.819452)   #0.005, 0.03

#diffuse priors
#for (j in 1:3){b[j]~dnorm(0,0.001)}
#b0~dnorm(-5,0.001)

#change1
#sigma1~dunif(0,5)
#sigma2~dunif(0,3)

#change2
#sigma1~dunif(0,9)
#sigma2~dunif(0,2)


#odds ratio
for (j in 1:3){or[j] <- exp( b[j] )}
```

}

y[]	hs[]	region[]		calfgrz[]	heifer[]	hf[]
14	210	2	1	0	1	
13	151	2	1	0	0	
14	476	2	1	0	1	
9	270	2	1	1	0	
9	505	2	0	0	0	
…						

OpenBUGS code for mixed effects beta regression model

```
Model{
for (j in 1:3){w[j]~dnorm(0,tau)}            #region level random effect
tau~dgamma(1,1)                    #place prior on precision

for (i in 1:100) {
  z[i] ~ dbeta(alpha[i], beta[i])          #prob of DD lesion+ ~ beta dist
  alpha[i] <- mu[i] * phi
  beta[i]  <- (1-mu[i]) * phi          #re-parameterize alpha and beta using mu and phi

#regn: region, the rest same to the first model code
  logit(mu[i]) <- b[1] + b[2]*calfgrz[i]+ b[3]*heifer[i]+w[regn[i]]
}
phi ~ dgamma(1,1)     #prior for phi
for (i in 1:3){b[i]~dnorm(0,0.01)}      #prior for regression coef

}
```

regn[]	z[]	calfgrz[]	heifer[]
3	0.7421	1	0
3	0.2361	1	0
3	0.3018	0	0
3	0.9977	1	1
3	0.9987	1	1
...			

OpenBUGS code for fixed effect beta regression model

```
Model{
phi ~ dgamma(1,1)
for (i in 1:5){b[i]~dnorm(0,0.01)}
for (i in 1:100) {
  z[i] ~ dbeta(alpha[i], beta[i])
  alpha[i] <- mu[i] * phi
  beta[i]  <- (1-mu[i]) * phi
#can and wai: dummy variables for Canterbury and Waikato regions
  logit(mu[i]) <- b[1] + b[2]*calfgrz[i]+ b[3]*heifer[i]+b[4]*can[i]+b[5]*wai[i]
}

#pred prob
#manawatu
pr[1]<-ilogit(b[1])
pr[2]<-ilogit(b[1]+b[2])
pr[3]<-ilogit(b[1]+b[2]+b[3])
pr[4]<-ilogit(b[1]+b[3])

#can
pr[5]<-ilogit(b[1]+b[4])
pr[6]<-ilogit(b[1]+b[2]+b[4])
pr[7]<-ilogit(b[1]+b[2]+b[3]+b[4])
pr[8]<-ilogit(b[1]+b[3]+b[4])

#wai
pr[9]<-ilogit(b[1]+b[5])
pr[10]<-ilogit(b[1]+b[2]+b[5])
pr[11]<-ilogit(b[1]+b[2]+b[3]+b[5])
pr[12]<-ilogit(b[1]+b[3]+b[5])


}
```

z[]	calfgrz[]	heifer[]	can[]	wai[]
0.7421	1	0	0	1
0.2361	1	0	0	1
0.3018	0	0	0	1
0.9977	1	1	0	1
0.9987	1	1	0	1

…

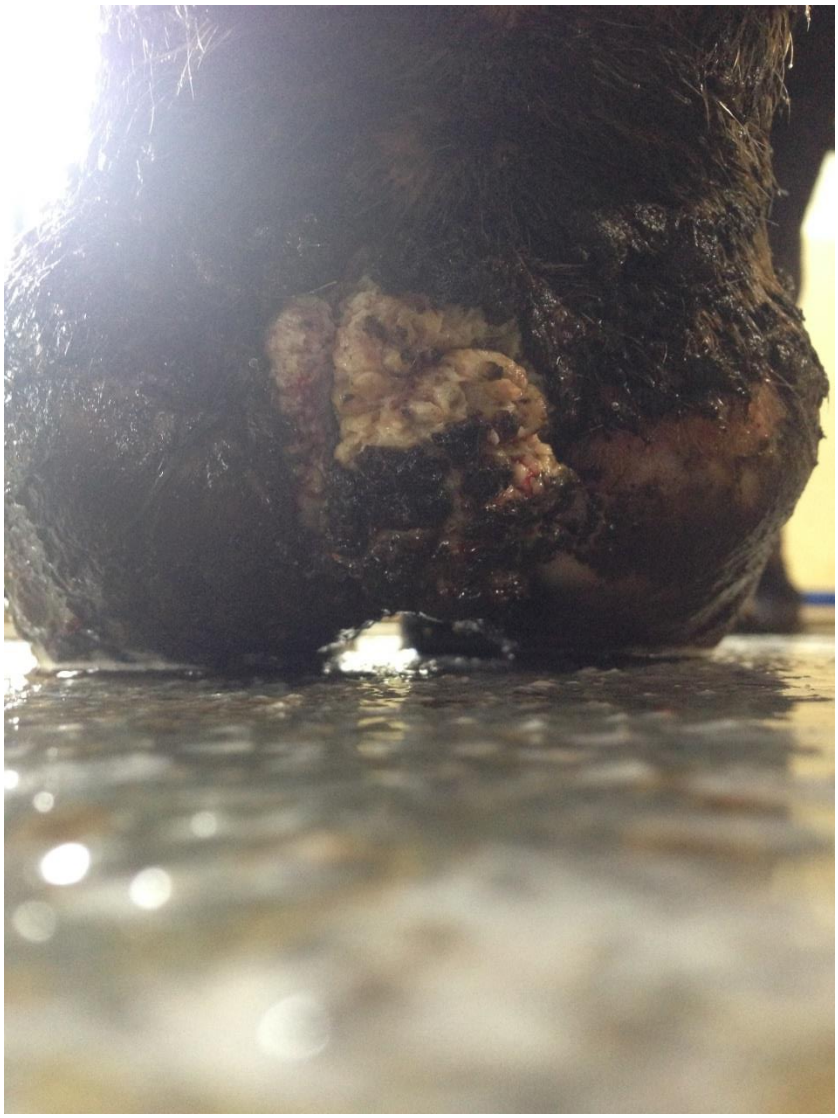
Additional file 3 for Yang DA, Gates MC, Müller KR and Laven RA. "Bayesian analysis of herd-level risk factors for bovine digital dermatitis in New Zealand dairy herds". BMC Vet Research.

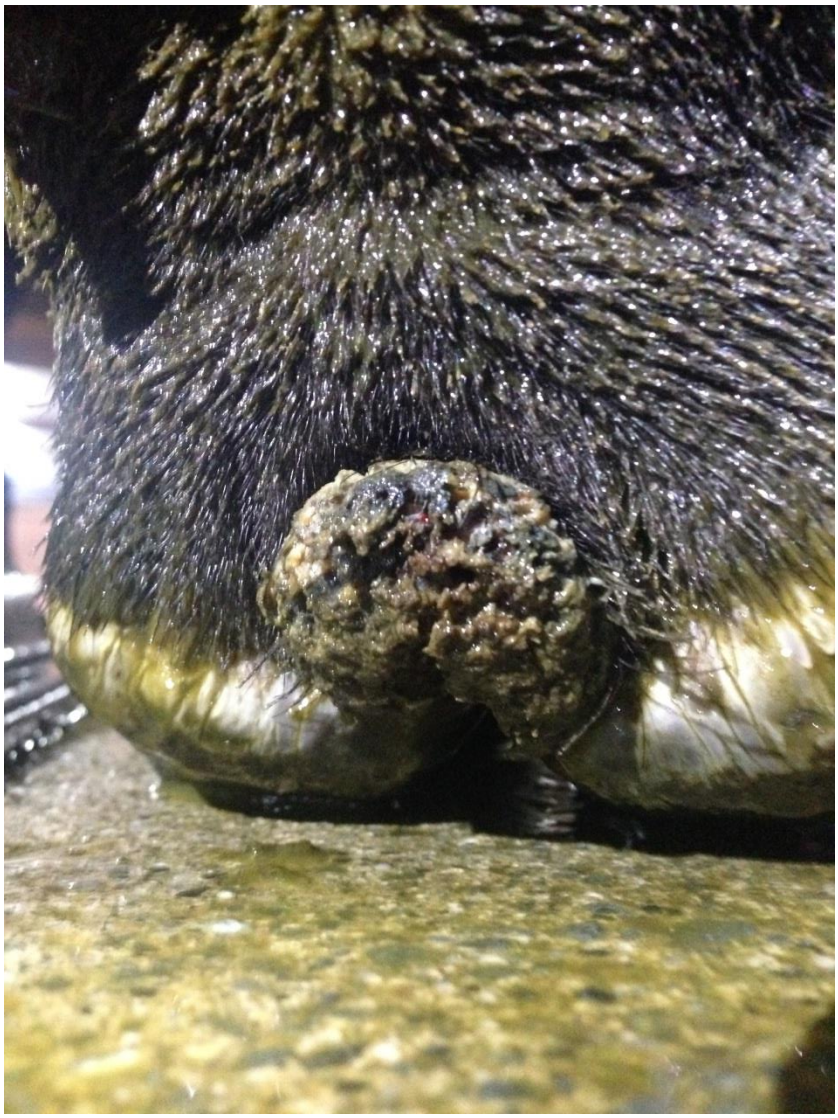
Results of the sensitivity analysis for binomial model

			Model			
	mean	sd	MC_error	val2.5pc	median	val97.5pc
β_0	-7.678	0.615	0.014	-8.896	-7.674	-6.462
β_1	1.327	0.400	0.006	0.548	1.324	2.126
β_2	1.061	0.363	0.004	0.356	1.056	1.782
β_3	0.782	0.417	0.005	-0.038	0.780	1.605
σ_U	2.303	0.460	0.002	1.331	2.359	2.968
σ_W	1.425	0.172	0.001	1.119	1.414	1.795
			Sensitivity analysis 1			
	mean	sd	MC_error	val2.5pc	median	val97.5pc
β_0	-8.076	1.236	0.064	-10.650	-8.054	-5.707
β_1	1.339	0.413	0.010	0.553	1.325	2.183
β_2	1.097	0.386	0.006	0.355	1.091	1.867
β_3	0.792	0.426	0.010	-0.042	0.790	1.644
σ_U	2.370	0.437	0.006	1.406	2.438	2.973
σ_W	1.433	0.176	0.002	1.120	1.422	1.813
			Sensitivity analysis 2			
	mean	sd	MC_error	val2.5pc	median	val97.5pc
β_0	-7.725	0.656	0.028	-8.994	-7.729	-6.423
β_1	1.331	0.405	0.010	0.528	1.334	2.123
β_2	1.049	0.365	0.007	0.343	1.045	1.775
β_3	0.756	0.422	0.010	-0.064	0.756	1.596
σ_U	3.222	0.953	0.005	1.510	3.200	4.884
σ_W	1.431	0.179	0.002	1.119	1.417	1.820
			Sensitivity analysis 3			
	mean	sd	MC_error	val2.5pc	median	val97.5pc
β_0	-7.572	0.651	0.027	-8.840	-7.571	-6.294
β_1	1.317	0.399	0.010	0.533	1.314	2.111
β_2	1.085	0.368	0.007	0.375	1.082	1.827
β_3	0.782	0.429	0.010	-0.055	0.783	1.632
σ_U	4.329	1.888	0.012	1.595	3.977	8.473
σ_W	1.429	0.175	0.002	1.120	1.418	1.806

Appendix 5: Additional files for Chapter 6

Schedule	Herd 1	Herd 2	Herd 3
First visit	21/Aug/2017	22/Aug/2017	22/Aug/2017
August 2017	2	2	2
September 2017	1	1	1
October 2017	4	4	4
November 2017	3	3	3
December 2017	2	1	1
January 2018	1	1	1
February 2018	0	0	0
March 2018	3	3	3
April 2018	3	1	2
Final visit	30/Apr/2018	03/Apr/2018	24/Apr/2018





Appendix 6: Published article: Inter-observer agreement between two observers for bovine digital dermatitis identification in New Zealand using digital photographs

Appendix 7: Published article: Detecting bovine digital dermatitis in the milking parlour: To wash or not to wash, a Bayesian superpopulation approach

Appendix 8: STATEMENT OF CONTRIBUTION DOCTORATE WITH PUBLICATIONS/MANUSCRIPTS

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We, the candidate and the candidate's Primary Supervisor, certify that all co-authors have consented to their work being included in the thesis and they have accepted the candidate's contribution as indicated below in the *Statement of Originality*.

Name of candidate:	Danchen Yang
Name/title of Primary Supervisor:	Prof. Richard Laven
Name of Research Output and full reference:	
Yang, D.A., Laven, R.A., Heuer, C., Vink, W.D., Chesterton, R.N., 2018. Farm level risk factors for bovine digital dermatitis in Taranaki, New Zealand: An analysis using a Bayesian hurdle model. The Veterinary Journal 234, 91-95.	
In which Chapter is the Manuscript /Published work:	Chapter 2
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Name of Research Output and full reference:	
Yang, D.A., Laven, R.A., Chesterton, R.N., 2019. Effects of climate and farm management practices on bovine digital dermatitis in spring-calving pasturebased dairy farms in Taranaki, New Zealand. The Veterinary Journal 247, 75- 80.	
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Name of Research Output and full reference:	
Yang, D.A., Johnson, W.O., Müller, K.R., Gates, M.C., Laven, R.A., 2019. Estimating the herd and cowlevel prevalence of bovine digital dermatitis on NewZealand dairy farms: A Bayesian superpopulation approach. Preventive Veterinary Medicine 165,	
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Name of Research Output and full reference:	
Yang, D.A., Gates, M.C., Müller, K.R., Laven, R.A., 2019. Bayesian analysis of herd-level risk factors for bovine digital dermatitis in New Zealand dairy herds. BMC Veterinary Research 15, 125.	
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Modelling the infection dynamics of bovine digital dermatitis in New Zealand pastoral dairy production systems	
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Name of Research Output and full reference:	
Yang, D.A., Laven, R.A., 2019. Inter-observer agreement between two observers for bovine digital dermatitis identification in New Zealand using digital photographs. New Zealand Veterinary Journal 67, 143-147.	
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Name of Research Output and full reference:	
Yang, D.A., Laven, R.A., 2019. Detecting bovine digital dermatitis in the milking parlour: To wash or not to wash, a Bayesian superpopulation approach. The Veterinary Journal 247, 38-43.	
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